



Oral Interventions for Obstructive Sleep Apnea

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Abstract: **BACKGROUND** The effectiveness of intraoral appliances (IOA), maxillary expansion (ME), and maxillomandibular advancement (MMA) in the treatment of children and adults with obstructive sleep apnea (OSA) has not yet been adequately assessed. **METHODS** An umbrella review was performed based on established guidelines for evidence-based medicine. Data synthesis was performed only from randomized controlled trials with Paule-Mandel random-effects meta-analyses / meta-regressions using mean differences (MDs) and 95% confidence intervals (CIs) and was followed by the qualitative evaluation of the meta-evidence. **RESULTS** 29 systematic reviews were included, 7 of which provided quantitative data. IOA were effective in improving apnea hypopnea index (AHI) compared to both, placebo appliances (12 trials; 525 patients; MD = -11.70; 95% CI: [-15.38; -8.01]; $p < 0.001$) and no treatment (1 trial; 24 patients; MD = -14.30; [-21.59; -7.01]; $p < 0.001$). Only the former comparison was supported by robust meta-evidence. Effectiveness of IOA as measured by the Epworth Sleepiness Scale, on the other hand, was not supported by robust meta-evidence. No randomized or prospective controlled trials were found on the effectiveness of ME (conventional or surgically assisted) and MMA. **CONCLUSION** Intraoral appliances are effective in reducing AHI and their use is substantiated by robust evidence. There is no evidence from high-quality research to support treatment with ME (conventional or surgically assisted) or MMA in patients with OSA.

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Oral interventions in obstructive sleep apnea

An umbrella review for the effectiveness of oral appliances, maxillary expansion, and maxillomandibular advancement

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SUMMARY

Background: Obstructive sleep apnea (OSA) affects 1-4% of children and 3-7% of adult population. Effectiveness of oral appliances (OA), maxillary expansion (ME), and maxillomandibular advancement (MMA) in the treatment of OSA has not yet been adequately assessed in an evidence-based manner in children and adults.

Method: An umbrella review was performed based on Cochrane Handbook and PRISMA statement to provide an overview of existing systematic reviews. Data synthesis was performed only from randomized controlled trials with Paule-Mandel random-effects meta-analyses / meta-regressions using Mean Differences (MDs) and 95% Confidence Intervals (CIs) and was followed by the qualitative evaluation of the meta-evidence.

Results: 29 systematic reviews were included (until August 2016), 7 of which provided quantitative data and 20 primary studies (until 2015). OA were effective in improving apnea hypopnea index (AHI) compared to both placebo appliances (12 trials; 525 patients; MD=-11.70; 95% CI=-15.38,-8.01; $p<0.001$) and no treatment (1 trial; 24 patients; MD=-14.30; 95% CI=-21.59,-7.01; $p<0.001$). Only the former was supported by robust meta-evidence. Effectiveness of OA compared to placebo on Epworth sleepiness scale and minimum oxygen saturation was low and moderate, respectively, and was not supported by robust meta-evidence. No randomized or prospective controlled trials were found on the effectiveness of ME (conventional or surgically assisted) and MMA.

Conclusion: OA are effective in reducing AHI and their use is substantiated by robust evidence. Treatment with ME (conventional or surgically assisted) and MMA cannot yet be supported by high quality research.

The clinical aspect

Oral appliances (OA) for the treatment of obstructive sleep apnea (OSA) work mechanically, by holding and stabilizing the mandible in a forward position and thus increasing the upper airway dimensions. Custom OA based on dental impressions are believed to be more effective than non-custom ones and cooperation with a qualified dentist / orthodontist is desired. OA are usually used in mild to moderate OSA patients and severe OSA patients, who cannot tolerate continuous positive airway pressure.

Rapid maxillary expansion to treat maxillary constriction can be performed in growing children by orthodontists. It opens the midpalatal suture and leads to a transverse expansion of the maxilla. Apart from the benefits of a balanced occlusion, this increases the nasopharyngeal airway and reduces nasal resistance facilitating nasal breathing. It is also believed that it leads to repositioning of the tongue anteriorly.

Surgically assisted rapid maxillary expansion to treat maxillary constriction is performed in adults by maxillofacial surgeons and orthodontists cooperatively. In adults, due to the ossification of the midpalatal suture, maxillary expansion has to be surgically assisted to maximize skeletal changes, otherwise it leads to dentoalveolar compensation (tipping of teeth). Adults enjoy the same treatment benefits as children.

Maxillomandibular advancement (MMA) is performed in adults by maxillofacial surgeons in cooperation with orthodontists. It advances the maxillomandibular complex in the sagittal plane thereby increasing the dimensions of the upper airway and the tone of the pharyngeal muscles. MMA is not a routine treatment in OSA and has to be anatomically indicated and carefully planned. Cephalometric analyses provide crucial help in identifying the anatomical site(s) of obstruction and in defining the limits of advancement to preserve facial aesthetics postoperatively.

Introduction

Obstructive sleep apnea (OSA) is a sleep-related disorder and refers to the repetitive narrowing or collapse of the upper airway, which leads to partial (hypopnea) or complete (apnea) cessation of the airflow during sleep (1). OSA is a common medical condition that affects 1% to 4% of children with a higher prevalence in boys than girls (2) as well as 2% to 5% of adult female and 3% to 7% of adult male population (3).

Risk factors for OSA development are characteristics and conditions, such as posterior position of the mandible (4, 5), obesity (6, 7), menopause (8, 9), high nasal airway resistance (10, 11), and smoking (12, 13). An overview of OSA pathophysiology and associated risk factors is given in *Figure 1* adapted from Jordan *et al.* (14). Since some well-established risk factors have a genetic background, OSA aggregates within families (15). However, susceptibility to OSA among family members is not fully explained by familial aggregation of other risk factors, such as obesity (16, 17).

The impact of OSA on patients is considerable. Lack of energy seems to be the most important complaint (18), although daytime sleepiness is also reported by 46%-47% of OSA patients (18, 19). Additionally, OSA sufferers have an elevated risk of motor vehicle crashes, although the actual number of accidents is not so frequent (20). Furthermore, their cognitive performance is impaired and that is related to OSA severity (21, 22), while their perceived quality of life appears to resemble that of other chronic diseases (23).

Available symptomatic or causative treatments include lifestyle interventions -especially weight loss, oral appliances (OA), continuous positive airway pressure (CPAP), pharmacological agents, and surgery (24, 25). Additionally, in orthodontics, maxillary expansion has been thought to increase the upper airway dimensions and thus alleviate OSA symptoms (26). Overall, dental science is implicated in many OSA treatment modalities including OA, rapid maxillary expansion (RME) in children, surgically assisted rapid maxillary expansion (SARME) in adults, and surgical maxillomandibular advancement (MMA) (24–30).

Here, we aimed to comparatively investigate the effectiveness of OSA treatment modalities for children and adults that are of interest to dentists / orthodontists by conducting an umbrella review of systematic reviews. Furthermore, we intended to systematically assess evidence on these interventions and to identify potential biases that could affect their findings.

Materials and methods

Protocol, registration, conduction, and reporting

The protocol for this study was made *a priori* and registered in PROSPERO (CRD42016045840). All *post hoc* changes are appropriately mentioned. The review was conducted according to the Cochrane Handbook (31) and reported according to the PRISMA statement (32). Guidelines provided by Aromataris *et al.* (33) were also considered.

Eligibility criteria, study identification and selection

Three search queries were created and appropriately adjusted to each electronic database systematically searched from inception to August 14th, 2016 (*eTable 1*). Firstly, systematic reviews were checked for inclusion according to the eligibility criteria for systematic reviews (*eTable 2*). Secondly, all primary studies of each included systematic review were extracted and checked according to the eligibility criteria for primary studies (*eTable 2*). A detailed description is provided in *eMethods*.

Data extraction

From each eligible systematic review, two authors (VK and SNP) extracted independently information. For further data extraction, we only considered the included systematic reviews, in which meta-analyses with comparison groups were provided. If an article presented separate meta-analyses on more than one eligible outcomes, those were assessed separately. Data extraction was based on the results provided in the included systematic review. In cases of discrepancies across systematic reviews, we directly extracted data from their corresponding primary studies. Additionally, data for the predefined subgroup analyses was directly extracted from primary studies. Further details are provided online (*eMethods*).

Assessment of summary effects and heterogeneity

For meta-analyses of continuous outcomes, Mean Differences (MDs) of the treatment-induced increments were chosen as effect estimates, while Risk Ratios (RRs) were chosen for binary outcomes. Based on clinical and statistical reasoning (e3), we estimated the summary effects with a random-effects model using the Paule-Mandel estimator instead of the commonly used DerSimonian-Laird, due to the improved performance of the former (e4). All calculations were performed in STATA version 12 (StataCorp, College Station, TX, USA). Further details on assessment of summary effects

and heterogeneity, assessment of small study effects, and criteria for epidemiological associations are provided in *eMethods*.

Results

Characteristics of included systematic reviews

A total of 497 hits were received from the electronic searches (*eFigure 1*). After excluding inappropriate studies (*eTable 3*), a total of 29 systematic reviews were included. *Table 1* provides an overview of the characteristics of the included systematic reviews and *eBox 1* a detailed description.

Risk of bias and methodological adequacy

Table 1 reports on the assessment of risk of bias in the included systematic reviews and *eTable 4* provides results for their methodological adequacy. A detailed description is provided in *eBox 2*.

Summary effect sizes

From the included systematic reviews, 18 (62%) performed meta-analyses of any kind of studies. After applying the eligibility criteria to their corresponding primary studies (including primary studies with comparison groups and excluding inappropriate study designs), data from 7 systematic reviews based on 20 primary studies (*eTable 5*) were extracted. After removing duplicate primary trials and pooling, 8 meta-analyses of cumulative evidence could be conducted on the primary outcome apnea hypopnea index (AHI) and the secondary outcomes Epworth Sleepiness Scale (ESS) and minimum oxygen saturation (MOS). These pertained to comparisons of OA with placebo appliances, no treatment, or different appliances (custom OA based on impressions, pre-fabricated OA, or tongue suction OA) in the treatment of OSA in adults (*Table 2*). No comparisons on RME, SARME, and MMA were available.

As far as the comparison of OA versus placebo appliances is concerned (*Table 2; Figure 2*), a considerable improvement was evident with OA in AHI (MD=-11.7; 95% CI=-15.38, -8.01; $p<0.001$), small marginally non-significant effects were noticed on ESS (MD=-1.18; 95% CI=-2.38, 0.03; $p=0.055$), and moderate effects on MOS (MD=3.33; 95% CI=1.38, 5.28; $p=0.007$). High heterogeneity ($I^2>75\%$) was found in the meta-analyses of AHI and MOS. However, this posed a threat to the results only for the latter meta-analysis. For the former meta-analysis, the 95% prediction interval that incorporates existing heterogeneity was consistent to the left side of the forest plot. Additionally, compared to no treatment, OA were found effective in improving AHI (MD=-14.30; 95% CI=-21.59, -

7.01; $p < 0.001$ as continuous and $RR = 0.37$; 95% $CI = 0.15, 0.90$; $p = 0.029$ as binary outcome), but not in improving ESS (MD=-1.00; 95% $CI = -3.77, 1.77$; $p = 0.479$). Finally, as far as comparisons between different appliance designs are concerned, increased vertical opening (14 mm instead of 4 mm) did not influence AHI (MD=-2.00; 95% $CI = -6.51, 2.51$; $p = 0.385$) and significantly hampered improvement in ESS (MD=-6.00; 95% $CI = -8.41, -3.59$; $p < 0.001$). However, this was based on a single trial and additional evidence is needed before any conclusions can be drawn.

Associations meeting the epidemiological criteria

From the cumulative evidence on the performance of OA, only the large improvement in AHI compared to placebo appliances was supported by robust evidence, i.e. had adequate sample, heterogeneity was not an issue, the random-effects predictive intervals were consistent in favour of the intervention, and no signs of reporting biases were found (*Table 3*).

Discussion

This umbrella review of systematic reviews summarizes existing evidence from randomized trials on the effectiveness of OA, RME, SARME, and MMA in the treatment of OSA. A total of 29 systematic reviews were included in the qualitative synthesis, while eligible trials from 7 of these also contributed to the quantitative synthesis. Comparisons were available only for OA, since for RME, SARME, and MMA no high quality evidence was identified.

Considerable evidence indicated that OA are effective in treating OSA in adults and improving AHI compared to both placebo appliances and no treatment. The former comparison was the only one that met all the criteria for strong epidemiological associations (e42) indicating strength of evidence. By mechanically holding the mandible in a forward position, OA not only affect the anteroposterior dimension but also provoke an increase in the lateral diameter of the velopharynx (e43). In growing children with malocclusion, functional appliances for stimulating mandibular growth might alleviate OSA symptoms (e44, e45), but evidence is scarce and thus more research is needed. In regard to the secondary outcomes, OA might have a positive effect on ESS and MOS (*Table 2*). However, the epidemiological strength of the association (e42, e49) was poor, mostly due to the limited number of contributing studies.

As far as modifying factors on the effectiveness of OA are concerned, subgroup analyses and meta-regressions indicated that baseline AHI levels were significantly associated with the observed

AHI reduction (eTable 6). This could mean that patients with more severe OSA symptoms are more likely to experience greater improvements in AHI, while the same association between baseline severity and improvement of symptoms was also noticed for the effect of OA on MOS (eTable 7), but not ESS (eTable 8). Although there were some indications of small-study effects, this was not confirmed with the Egger's test. Furthermore, this association could also be explained by "regression to the mean" and needs further confirmation. It is also important to note, that OSA baseline severity might directly influence treatment choices (30) leading to OA being used more in mild to moderate cases with non-compliance to CPAP, since CPAP appears to be more effective in complete resolution of OSA compared to OA (28). Although OA are not as effective as the first-line option, CPAP, in reducing AHI (e46, e47), they might be better preferred by patients, since CPAP is associated with more serious negative aspects, which influence adherence (e47, e48) and thus treatment effectiveness. Due to this fact, OA could be used alternatively to CPAP in mild to moderate OSA and in severe OSA, if CPAP is not tolerated (30).

Although RME, SARME, and MMA in the treatment of OSA could not be supported by robust evidence, existing literature could be suggestive of their effectiveness. In a randomized crossover trial comparing RME with adenotonsillectomy in children, AHI was reduced after RME in the first arm of the trial (e50). Moreover, it seems that this reduction remains stable after 36 months (e51). In adults, SARME with mini-implants reduced AHI postoperatively (e52). Finally, although existing literature on MMA is mainly comprised by inappropriate study designs, MMA seems to be as effective as CPAP with AHI pre- and postoperatively comparable to AHI pre- and post-CPAP (e53).

Strengths and weaknesses

Firstly, the present umbrella review was based on robust methodology (e42, e49) that was set out *a priori* and registered in PROSPERO (e54). Secondly, study selection and data extraction were also based on the level of primary studies included in the identified systematic reviews. As a result, this report synthesized only randomized trials (since no prospective controlled trials were found) and accuracy of the data was insured. Thirdly, the Paule-Mandel estimator of random-effects model was used as it outperforms the DerSimonian-Laird variance estimator (e4). Finally, the robustness of existing cumulative meta-evidence was judged on basis of valid protocols of epidemiological strength (e42, e49).

On the other hand, several limitations should be considered in the interpretation of our findings. Firstly, we might have missed some individual studies, if those were not identified in the original systematic reviews. Secondly, most of the included systematic reviews presented serious methodological inadequacies. Thirdly, funnel plot asymmetry was consistently investigated with Egger's test for all meta-analyses according to previous umbrella reviews (e42, e49, e55), although less than ten trials were included in every case (e9).

Key messages

- According to criteria for robust epidemiological associations, OA are effective in reducing AHI in OSA adult patients and this cannot be explained by placebo effects.
- The epidemiological evidence for the effect of OA on ESS and MOS in OSA adult patients was poor.
- There is no robust scientific evidence to support the treatment of RME, SARME, and MMA in OSA patients.

Conflict of interest statement

The authors declare that no conflict of interest exists.

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- e35. Ramar K, Dort LC, Katz SG, et al.: Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015. *J Clin Sleep Med* 2015; 11: 773–827.
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Tables

Table 1. Characteristics of included systematic reviews.

| Nr. | Systematic review | Databases searched | Tx | Internal validity | Outcomes *1 | MA | Evidence quality | Conflict of Interest |
|-----|--------------------------------------|----------------------|--------|----------------------------|------------------------|-----|------------------|--|
| 1 | Abdullatif (2016) (e11) | 9 | ME | NICE tool | AHI, LOS | Yes | No | NR |
| 2 | Ahrens (2011) (e12) | 4 | OA | AASM criteria | AHI, RDI | No | No | External, non-profit |
| 3 | Bartolucci (2016) (e13) | 6 | OA | EPHPP tool | AHI | Yes | GRADE | None existing |
| 4 | Bratton (2015) (e14) | 2 | OA | Cochrane RoB | ESS | Yes | No | External / internal non-profit |
| 5 | Bridgman and Dunn (2000) (e15) | 4 | MMA | Jadad scale | OD | No | No | External, non-profit |
| 6 | Caldas (2009) (e16) | 1 | OA | Jadad scale | AHI, ESS, OD | No | No | NR |
| 7 | Camacho (2015) (e17) | 4 | MMA | NICE tool | AHI, RDI, ESS, LOS | Yes | No | External, non-profit |
| 8 | Caples (2010) (e18) *2 | 4 | MMA | NR | AHI | Yes | GRADE | External for one author, research support from ResMed and Ventus Medical |
| 9 | Carvalho (2007, 2016) (e19, e20) | 6 | OA | Cochrane RoB | AHI | No | GRADE | External, non-profit |
| 10 | Health Quality Ontario (2009) (e21) | 6 | OA | Custom (Goodman) | AHI, ESS | Yes | GRADE | None existing |
| 11 | Hoekema (2004) (e22) | 4 | OA | Custom (e41) | AHI, ESS | Yes | No | External, non-profit |
| 12 | Holty and Guilleminault (2010) (e23) | 1 | MMA | - | AHI, ESS, LOS, SE | Yes | No | None existing |
| 13 | Hsieh and Liao (2013) (e24) | 1 | MMA | Jadad scale | AHI | No | No | External, non-profit |
| 14 | Huynh (2016) (e25) | 4 | OA, ME | ARRIVE (modif. for humans) | AHI, OS | Yes | No | None existing |
| 15 | Knudsen (2015) (e26) | 2 | MMA | - | AHI, LOS | Yes | No | None existing |
| 16 | Li (2013) (e27) | 3 | OA | Cochrane RoB | AHI, ESS, LOS | Yes | No | None existing |
| 17 | Lim (2004) (e28) | 2 | OA | Jadad scale | AHI, LOS | Yes | No | External, non-profit |
| 18 | Machado-Júnior (2016) (e29) | 1 | ME | - | AHI | Yes | No | None existing |
| 19 | Marcus (2012) (e30) | 6 | ME | AAN criteria | AHI | No | AAP criteria | None existing |
| 20 | Marklund (2012) (e31) | 2 | OA | CEBM criteria | AHI, ESS, OS | No | CEBM criteria | None existing |
| 21 | Nazarali (2015) (e32) | 6 | OA | Cochrane RoB | AHI, OD | No | No | NR |
| 22 | Okuno (2014) (e33) | 3 | OA | Cochrane RoB (modif.) | AHI, ESS | Yes | GRADE | None existing |
| 23 | Pirklbauer (2011) (e34) | 1 | MMA | CEBM criteria | AHI, ESS | No | No | NR |
| 24 | Ramar (2015) (e35) | 2 | OA | Cochrane RoB (modif.) | AHI, RDI, ESS, LOS, SE | Yes | GRADE | External for some authors, profit / non-profit |
| 25 | Serra-Torres (2016) (e36) | 3 | OA | CONSORT | AHI, ESS, OS | No | No | None existing |
| 26 | Sharples (2016) (e37) | 3 & existed databank | OA | Jadad scale | AHI, ESS | Yes | No | None existing |
| 27 | Sher (1996) (e38) | 1 | MMA | - | AHI, LOS | No | No | NR |
| 28 | Zaghi (2016) (e39) | 4 | MMA | NR | AHI, RDI | Yes | No | None existing |
| 29 | Zhu (2015) (e40) | 5 | OA | Cochrane RoB | AHI, ESS, LOS, SE | Yes | GRADE | External, non-profit |

AAN, American Academy of Neurology; AAP, American Academy of Pediatrics; AASM, American Academy Sleep Medicine; AHI, apnea hypopnea index; CEBM, Center for Evidence-Based Medicine in Oxford; EPHPP, Effective Public Health Practice Project; ESS, Epworth Sleepiness Scale; LOS, lowest oxygen saturation; MA, meta-analysis; ME, maxillary expansion; MMA, maxillomandibular advancement; NR, not reported; OA, oral appliance; OD, oxygen desaturation; OS, oxygen saturation; RDI, respiratory disturbance index; SE, sleep efficiency; Tx, treatment.

*1 Only among those included in our study protocol

*2 Data extracted only on MMA

Table 2. Results of available comparisons regarding the primary and secondary outcomes.

| | | | | | | | Heterogeneity | | | | Largest trial | Egger's test |
|--|----------------------------------|--------|-------|---------------------------|---------|-------|---------------|-------|----------|------------|----------------------|--------------|
| | Outcome | Trials | Pat's | Effect (95% CI) | p value | Sign. | τ^2 | I^2 | Comment | Consistent | Effect (95% CI) | Sign. |
| Oral appliance versus placebo appliance | | | | | | | | | | | | |
| A | AHI _{con} ^{*1} | 12 | 525 | MD: -11.7 (-15.38,-8.01) | <0.001 | ** | 20.2 | 93.6% | High | Yes | -9.3 (-12.00, -6.60) | NS |
| B | ESS ^{*2} | 11 | 475 | MD: -1.18 (-2.38,0.03) | 0.055 | | 2.1 | 60.6% | Moderate | No | -2.01 (-2.70,-1.32) | NS |
| C | Min satur ^{*3} | 6 | 286 | MD: 3.33 (1.38,5.28) | 0.007 | * | 2.2 | 96.8% | High | Yes | 1.90 (0.51,3.29) | - |
| Oral appliance versus no appliance | | | | | | | | | | | | |
| D | AHI _{con} | 1 | 24 | MD: -14.30 (-21.59,-7.01) | <0.001 | ** | - | - | - | - | Same | - |
| E | AHI _{bin} | 1 | 23 | RR: 0.37 (0.15,0.90) | 0.029 | * | - | - | - | - | Same | - |
| F | ESS | 1 | 23 | MD: -1.00 (-3.77,1.77) | 0.479 | | - | - | - | - | Same | - |
| Oral appliance ₁ versus oral appliance ₂ | | | | | | | | | | | | |
| G | AHI | 1 | 23 | MD: -2.00 (-6.51,2.51) | 0.385 | | - | - | - | - | Same | - |
| Oral appliance ₁ versus oral appliance ₂ | | | | | | | | | | | | |
| H | ESS | 1 | 67 | MD: -6.00 (-8.41,-3.59) | <0.001 | ** | - | - | - | - | Same | - |

CI, Confidence Intervals; MD, Mean Differences; AHI, apnea hypopnea index; Min Satur, minimum oxygen saturation; ESS, Epworth Sleepiness Scale; con, continuous; bin, binary; oral appliance₁, oral appliance with 4 mm opening; oral appliance₂, oral appliance with 14 mm opening

^{*1} 95% Predictive Intervals; Estimate: -22.55,-0.85; Consistent: Yes

^{*2} 95% Predictive Intervals; Estimate: -4.76,2.40; Consistent: No

^{*3} 95% Predictive Intervals; Estimate: -1.62,8.28; Consistent: No

Table 3. Results on epidemiological criteria regarding the primary and secondary outcomes.

| | Outcome | p<0.001 | Adequate sample | Heterogeneity not a problem | PrI Consistent | Egger's test NS | Criteria met |
|--|--------------------|---------|-----------------|-----------------------------|----------------|--------------------|--------------|
| Oral appliance versus placebo appliance | | | | | | | |
| A | AHI _{con} | Yes | Yes | Yes | Yes | Yes | Yes |
| B | ESS | No | No | No | No | Yes | No |
| C | Min satur | No | No | Yes | No | - | No |
| Oral appliance versus no appliance | | | | | | | |
| D | AHI _{con} | Yes | No | - | - | - | No |
| E | AHI _{bin} | No | No | - | - | - | No |
| F | ESS | No | No | - | - | - | No |
| Oral appliance ₁ versus oral appliance ₂ | | | | | | | |
| G | AHI | No | No | - | - | - | No |
| H | ESS | Yes | No | - | - | - | No |

PrI, Predictive Intervals; NS, not significant; AHI, apnea hypopnea index; Min Satur, minimum oxygen saturation; ESS, Epworth Sleepiness Scale; con, continuous; bin, binary; oral appliance₁, oral appliance with 4 mm opening; oral appliance₂, oral appliance with 14 mm opening

Figure legends

Figure 1. Diagram summarizing the pathophysiology of obstructive sleep apnea [adapted from Jordan *et al.* (14) with permission].

Figure 2. Forest plot providing an overview of included meta-analyses and their results.

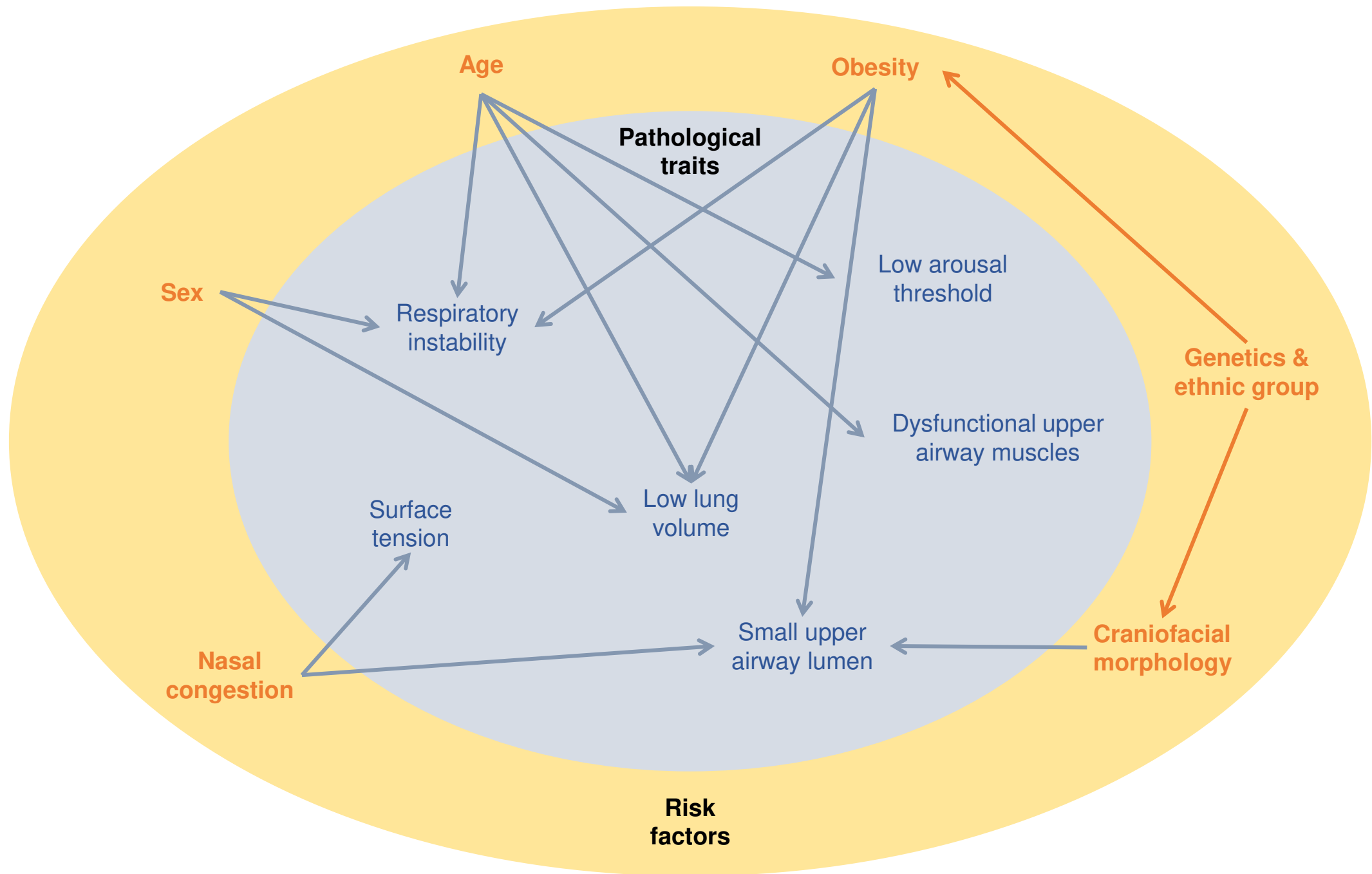
MD, Mean Differences; CI, Confidence Intervals; AHI, apnea hypopnea index; OA, oral appliances; OA₁ vs OA₂, oral appliance (4 mm opening) versus oral appliance (14 mm opening); ESS, Epworth Sleepiness Scale.

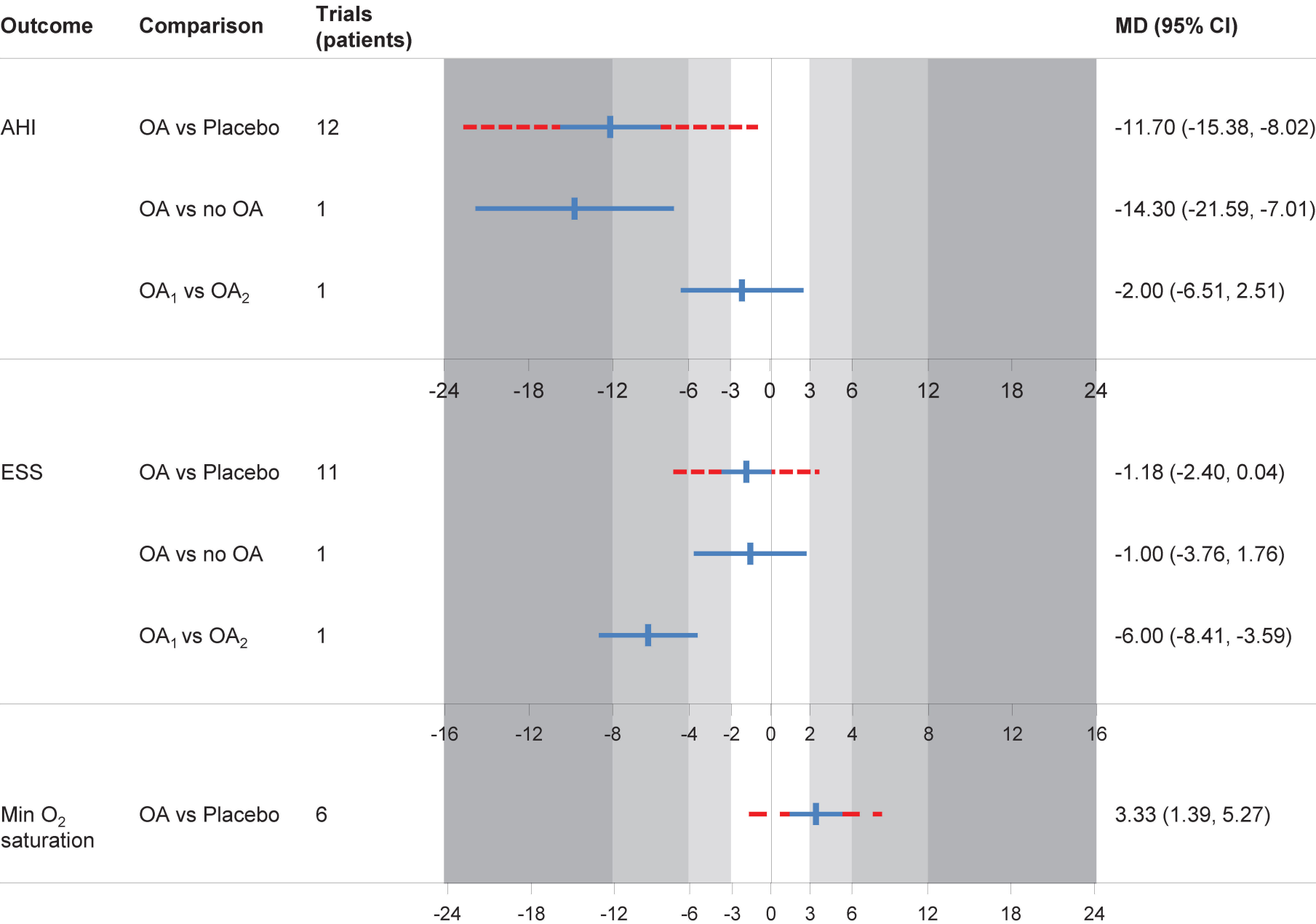
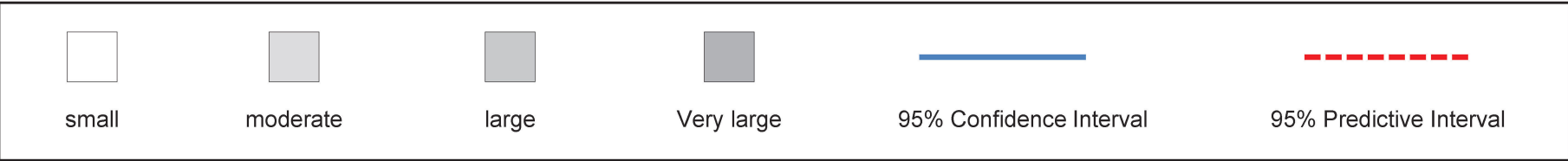
eFigure 1. Flow diagram for the selection of included studies.

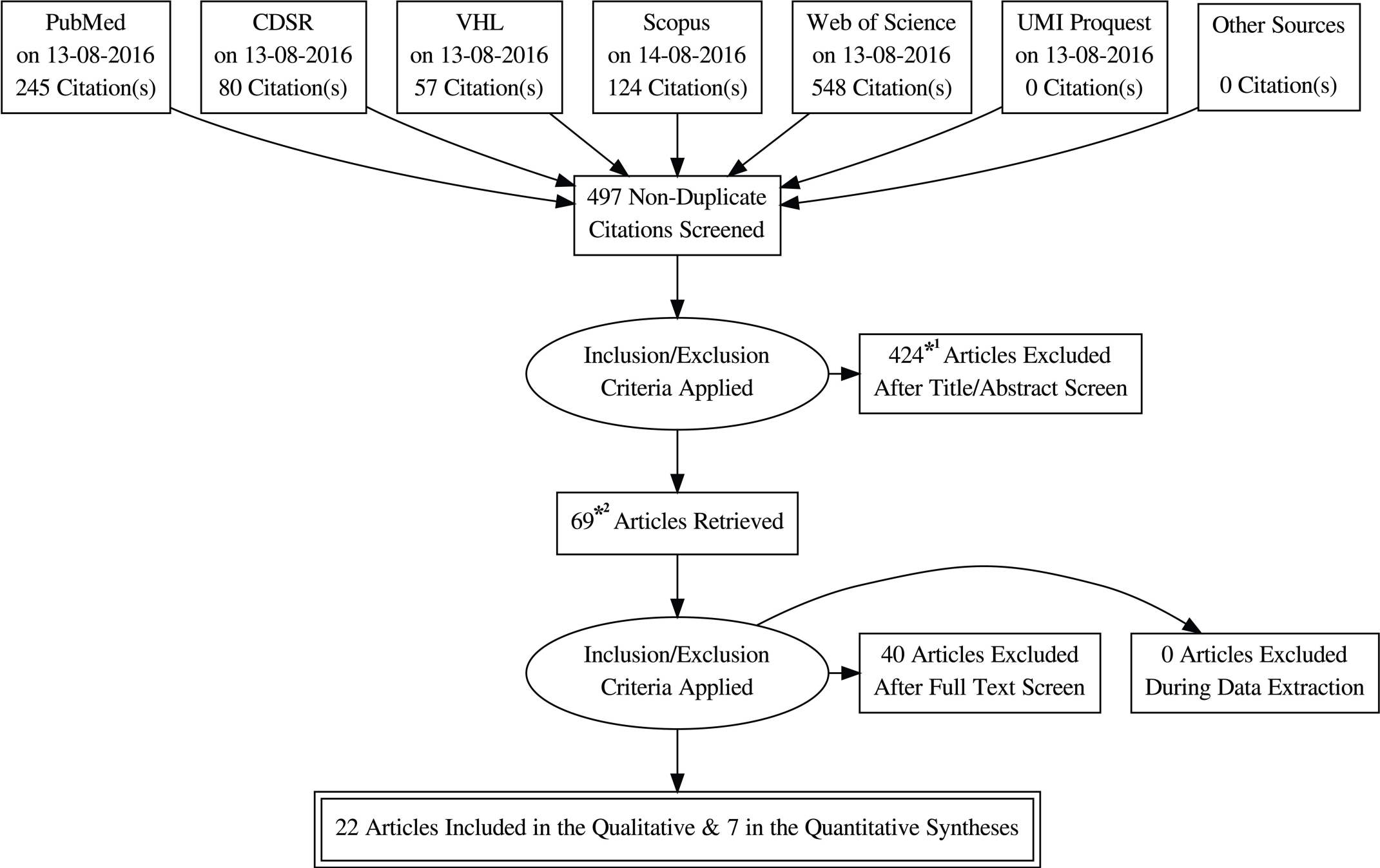
CDSR, Cochrane Database of Systematic reviews; VHL, Virtual Health Library.

*1 Three abstracts could not be found

*2 One full text could not be found







Supplementary material

eMethods

Eligibility criteria, study identification and selection

No limitations on publication date, language, and status were applied to our searches. Additional hand searches of the reference lists of eligible articles were undertaken. Finally, two electronic databases (Google Scholar and PROSPERO) were manually searched for additional systematic reviews and / or protocols.

Eligibility of systematic reviews was assessed on the basis of title, abstract, and full-text. Authors were contacted whenever a full-text could not be found. Study identification and selection were performed by one reviewer (VK) with a subsequent independent duplicate check by a second reviewer (SNP). Conflicts were resolved by discussion (TE).

For adults, OSA was defined as having an apnea-hypopnea index of at least five episodes per hour of sleep or a respiratory disturbance index of at least five episodes per hour of sleep (34). For children, OSA was defined as having an AHI of at least one episode per hour of sleep (35, 36). Primary trials included in systematic reviews had to be randomized clinical trials or prospective non-randomized controlled trials of any clinical setting. We excluded studies with retrospective or historical experimental and control groups as they are associated with bias (37, 38).

Data extraction

From each included systematic review, we recorded if the included systematic reviews assessed the risk of bias of the individual studies and the quality of evidence according to the GRADE approach (39), but we did not perform these procedures ourselves, as this task was beyond the scope of this umbrella review of systematic reviews. Additionally, we appraised the methodological quality of the included systematic reviews with the AMSTAR tool (40).

From each eligible meta-analysis, the same two authors extracted information independently on first author, year of publication, outcome examined, number of included studies, and reported data at the individual trial level. Eligible outcomes were extracted in either continuous or binary format. In order to deal with study overlaps across included meta-analyses, the PubMed Unique Identifier (PMID)

was used to characterize each trial included in the meta-analyses and all available trials were pooled according to PMID.

After checking for design suitability and lack or proper handling by the trialists of carry-over effects (31, e1), we decided to include and combine both parallel and crossover randomized trials, approximating a paired analysis for the latter. We extracted for each outcome the absolute increment of change through treatment as final minus baseline value. In case this was not reported in the original trials, we calculated this ourselves using appropriate methods for paired data (31), using a pre-post correlation of 0.50 from existing data (e2). For crossover trials, we additionally calculated the effect size by subtracting the increment of change from baseline of each trial arm using a similar paired approach (e1) and a correlation of 0.25, again, from existing data (e2).

Assessment of summary effects and heterogeneity

A random-effects synthesis makes the assumption that individual studies are estimating different effects, which are assumed to have a normal distribution. The random-effects meta-analysis is performed to estimate the mean of this distribution of effects across different studies and the uncertainty about that mean (95% Confidence Interval (CI)). Cut-offs of half, one, and two standard deviations of the response in the control group (taken from the largest included trials) were used to augment all forest plots with contours of effect magnitude.

We assessed heterogeneity between studies by calculating both the variance among effect sizes τ^2 and the I^2 metric of inconsistency, which could reflect either genuine diversity or bias (e5). The I^2 metric ranges between 0% and 100%, and is the ratio of variance between studies over the sum of the variances within and between studies. We also assessed descriptively whether heterogeneity would influence the direction or only magnitude of effects (i.e. if meta-analysed studies lay on both sides or on only one side of the forest plot, respectively) (e6). Finally, we calculated the 95% Prediction Interval (Prl) for the summary random-effects estimates, which further accounts for heterogeneity between studies and indicates the uncertainty for the effect that would be expected in a new study examining that same association (e7). The 95% Prl shows where the true effects are for 95% of the studies from the population of studies that are synthesized or similar (exchangeable) studies that might be performed in the future.

Predefined mixed-effects subgroup analyses and random-effects meta-regressions were performed for the following factors: baseline patient characteristics (including mean age, ratio of male patients, mean AHI, mean BMI, and sample size), follow-up time, % of maximum protrusion in the construction of oral appliances (OA), appliance category (custom OA based on impressions, pre-fabricated OA, tongue suction OA), and appliance type (1- or 2-piece). Sensitivity analyses were performed to assess any systematic differences according to study design (parallel or crossover) or data calculations done for this umbrella review.

Assessment of small study effects

We examined whether there is an indication for small study effects - that is, if small studies tend to give higher estimates than large studies. Small study effects can indicate publication bias or other reporting biases, but they can also reflect genuine heterogeneity, chance, or other reasons for differences between small and large studies (e8). We used the regression asymmetry test proposed by Egger *et al.* (e9) to investigate funnel plot asymmetry in meta-analyses of at least 10 studies (e8).

Associations meeting further criteria

We further identified associations for which the random-effects estimates showed strong evidence of significance according to the following criteria: (a) $p < 0.001$, a threshold that has been suggested to substantially reduce the number of false positive findings (e10), (b) associations based on adequate sample (>500 patients), (c) associations that did not have large heterogeneity between studies ($I^2 < 75\%$), which could affect the direction of estimates, (d) their 95% PrI excluded the null value, and (e) had no evidence of small study effects (from the Egger's test). All p values were two-sided, while statistical significance was set at 5% for all tests, except for heterogeneity and Egger's tests (10%). Although multiple p values are reported in this umbrella review, no correction or adjustment was performed, as we aimed to summarize the results of the included papers.

eBox 1

Characteristics of the included systematic reviews

- Twenty eight reviews were published in scientific journals, while one was published as a Health Technology Assessment.
- All reviews were published in English between 1996 and 2016 and searched from one to nine literature databases.
- Ten (34%) reviews included only RCTs, 7 (24%) included both RCTs and non-RCTs, and the remaining 12 (41%) only included non-RCTs.
- The majority of them (16 reviews; 55%) assessed oral appliances, 9 (31%) assessed surgical maxillomandibular advancement, 3 (10%) assessed maxillary expansion, and one assessed more than one intervention.
- Almost all of the reviews (27 reviews; 93%) reported on the primary outcome AHI, 14 (48%) reported on ESS, and 15 (52%) reported on oxygen saturation indices.
- From the included systematic reviews, 12 (41%) had no conflicts of interest, 9 (31%) declared non-profit support, 2 (7%) involved company support, and 6 (21%) did not declare any status.
- At the time of this umbrella review, 4 included reviews had not been cited, while the rest gathered in total 2980 citations in Google Scholar ® (median=21; range=1-1016)

eBox 2

Risk of bias and methodological adequacy of the included systematic reviews

- Out of the 29 included systematic reviews, 23 of them (79%) assessed the risk of bias in the included trials; seven of them (24%) with the Cochrane Collaboration's risk of bias tool.
- The quality of evidence (strength of recommendations) from the performed meta-analyses was assessed with the GRADE approach only in 7 out of 29 reviews (24%) and with other approaches in another 2 reviews (7%). The strength of recommendations of the included reviews ranged from very low to high.
- The AMSTAR scores for the included reviews ranged from 1 to 9 out of 11, with a mean score of 5 (excluding non-applicable ratings) and a standard deviation of 2, while no review scored full points.
- The main shortcomings were lack of *a priori* design (in 22 [76%] of the reviews), incomplete reporting of included / excluded studies (in 24 [83%] of the reviews), absence of grey literature searches (in 21 [72%] of the reviews), and missing statements for possible conflicts of interest (in all of the reviews).

eTable 1. Identification of studies. Databases, dates, search strategies, and hits.

| Database and date searched | Search query | Hits per query | Hits per database |
|---|---|----------------|-------------------|
| PubMed | (((((appliance OR device OR splint*)) AND (mandib* OR "lower jaw"))) AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) Filters: Review | 132 | 245 |
| http://www.ncbi.nlm.nih.gov/pubmed/advanced , on 13.08.2016 | (((((maxilla* OR palat*)) AND expansion) AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) Filters: Review | 43 | |
| | (((((("maxillomandibular advancement" OR osteotomy OR BSSO OR "bilateral sagittal split osteotomy" OR "mandibular advancement" OR "Le Fort" OR "maxillary advancement")) AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) Filters: Meta-Analysis; Systematic Reviews | 70 | |
| Cochrane Database of Systematic Reviews | (appliance or device or splint*) and (mandib* or "lower jaw") and ("obstructive sleep apnoea" or "obstructive sleep apnea" or OSA or apnea or apnoea or snor* or breath* or respir* or hypopnea or sleep*) in Cochrane Reviews (Search all text) | 46 | 80 |
| http://onlinelibrary.wiley.com/cochranelibrary/search , on 13.08.2016 | ("maxillary expansion" or "palatal expansion") and ("obstructive sleep apnoea" or "obstructive sleep apnea" or OSA or apnea or apnoea or snor* or breath* or respir* or hypopnea or sleep*) in Cochrane Reviews (Search all text) | 6 | |
| | ("maxillomandibular advancement" or osteotomy or BSSO or "bilateral sagittal split osteotomy" or "mandibular advancement" or "Le Fort" or "maxillary advancement") and ("obstructive sleep apnoea" or "obstructive sleep apnea" or OSA or apnea or apnoea or snor* or breath* or respir* or hypopnea or sleep*) in Cochrane Reviews (Search all text) | 28 | |
| Virtual Health Library | (tw:(appliance OR device OR splint*)) AND (tw:(mandib* OR "lower jaw")) AND (tw:(("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) AND (tw:(("systematic review" OR "meta-analysis")) in Title, abstract, subject | 16 | 57 |
| http://pesquisa.bvsalud.org/portal/advanced/?lang=en , on 13.08.2016 | (tw:(("maxillary expansion" OR "palatal expansion")) AND (tw:(("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) AND (tw:(("systematic review" OR "meta-analysis")) in Title, abstract, subject | 9 | |
| | (tw:(("maxillomandibular advancement" OR osteotomy OR BSSO OR "bilateral sagittal split osteotomy" OR "mandibular advancement" OR "Le Fort" OR "maxillary advancement")) AND (tw:(("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*)) AND (tw:(("systematic review" OR "meta-analysis")) in Title, abstract, subject | 32 | |
| Scopus | (TITLE-ABS-KEY ("maxillomandibular advancement" OR osteotomy OR bssso OR "bilateral sagittal split osteotomy" OR "mandibular advancement" OR "Le Fort" OR "maxillary advancement") AND TITLE-ABS-KEY ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR osa OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) AND TITLE-ABS-KEY ("systematic review" OR "meta-analysis")) | 61 | 124 |
| http://www.scopus.com/search/ , on 14.08.2016 | (TITLE-ABS-KEY ((((appliance OR device OR splint*)) AND (mandib* OR "lower jaw")) AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR osa OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*))) AND TITLE-ABS-KEY ("systematic review" OR "meta-analysis")) | 53 | |
| | (TITLE-ABS-KEY ((((maxilla* OR palat*)) AND expansion) AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR osa OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*))) AND TITLE-ABS-KEY ("systematic review" OR "meta-analysis")) | 10 | |
| Web of Science | TOPIC: (appliance OR device OR splint*) AND TOPIC: (mandib* OR "lower jaw") AND TOPIC: ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) Refined by: DOCUMENT TYPES: (REVIEW) All Databases | 208 | 548 |
| http://apps.webofknowledge.com/ , on 13.08.2016 | TOPIC: ("maxillary expansion" OR "palatal expansion") AND TOPIC: ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) Refined by: DOCUMENT TYPES: (REVIEW) All Databases | 64 | |
| | TOPIC: ("maxillomandibular advancement" OR osteotomy OR BSSO OR "bilateral sagittal split osteotomy" OR "mandibular advancement" OR "Le Fort" OR "maxillary advancement") AND TOPIC: ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) Refined by: DOCUMENT TYPES: (REVIEW) All Databases | 276 | |
| UMI Proquest | (appliance OR device OR splint*) AND (mandib* OR "lower jaw") AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) in Dissertations & Theses / Anywhere | 0 | 0 |
| http://search.proquest.com/advanced/reset?accountid=13478 , on 13.08.2016 | ("maxillary expansion" OR "palatal expansion") AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) in Dissertations & Theses / Anywhere | 0 | |
| | ("maxillomandibular advancement" OR osteotomy OR BSSO OR "bilateral sagittal split osteotomy" OR "mandibular advancement" OR "Le Fort" OR "maxillary advancement") AND ("obstructive sleep apnoea" OR "obstructive sleep apnea" OR OSA OR apnea OR apnoea OR snor* OR breath* OR respir* OR hypopnea OR sleep*) in Dissertations & Theses / Anywhere | 0 | |
| Sum | | | 1054 |

eTable 2. Eligibility criteria for selecting systematic reviews and primary studies.

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|---|
| 1. Criteria for including systematic reviews (with or without meta-analysis) |
| Inclusion criteria |
| At least one database is systematically searched and |
| There is at least a rudimentary systematic methodology, such as: methodological quality assessment of included studies with any tool or conduction of meta-analysis or study selection or data extraction in duplicate |
| Exclusion criteria |
| Systematic reviews of animal studies, narrative reviews, and practice guidelines based on literature search |
| 2. Criteria for selecting primary studies included in the systematic reviews |
| Inclusion criteria |
| Patients with <i>a priori</i> diagnosis of OSA (AHI ≥ 5 or RDI ≥ 5 for adults and AHI ≥ 1 for children) of any age or sex |
| OA, RME, SARME, and MMA to alleviate / treat OSA |
| Direct comparisons between two or more interventions or between patients receiving the intervention and untreated / placebo matched controls |
| Randomized controlled trials or prospective non-randomized clinical trials of parallel or crossover design |
| Any clinical setting |
| Primary outcome: AHI measured with polysomnography before and after the intervention |
| Secondary outcomes measured before and after the intervention: RDI, oximetry indices, sleep efficiency, REM sleep latency, and ESS |
| Exclusion criteria |
| Studies reporting on patients suffering from other than OSA conditions |
| Non-clinical studies, retrospective clinical studies, case series (less than 10 patients), and case reports |

OSA, obstructive sleep apnea; AHI, apnea hypopnea index; RDI, respiratory disturbance index, OA, oral appliance; RME, rapid maxillary expansion; SARME, surgically assisted rapid maxillary expansion; MMA, maxillomandibular advancement; REM, rapid eye movement; ESS, Epworth Sleepiness Scale

eTable 3. Selection of systematic reviews.

| Nr. | Citation | Exclusion based on | Reason |
|-----|---|--------------------|--------------|
| 1 | Aiello KD, Caughey WG, Nelluri B, Sharma A, Mookadam F & Mookadam M (2016): Effect of exercise training on sleep apnea: A systematic review and meta-analysis. <i>Respiratory Medicine</i> 116: 85–92. | title | Not relevant |
| 2 | Alessandri-Bonetti G, Ippolito DR, Bartolucci ML, D'Antò V & Incerti-Parenti S (2015): Cephalometric predictors of treatment outcome with mandibular advancement devices in adult patients with obstructive sleep apnea: a systematic review. <i>Korean J Orthod</i> 45: 308–321. | title | Not relevant |
| 3 | Annapurna K, Suganya S, Vasanth R & Kumar PR (2014): Prosthodontic approach to treat obstructive sleep apnea. <i>Annals of medical and health sciences research</i> 4: 481–6. | title | Not relevant |
| 4 | Atkeson A, Yeh SY, Malhotra A & Jelic S (2009): Endothelial Function in Obstructive Sleep Apnea. <i>Progress in Cardiovascular Diseases</i> 51: 351–362. | title | Not relevant |
| 5 | Attanasio R (1997): An overview of bruxism and its management. <i>Dent Clin North Am</i> 41: 229–241. | title | Not relevant |
| 6 | Bacher M, Linz A, Buchenau W, Arand J, Krimmel M & Poets C (2010): Treatment of Infants with Pierre Robin Sequence. <i>Laryngo-Rhino-Otologie</i> 89: 621–627. | title | Not relevant |
| 7 | Bagnall A-M, Jones L, Duffy S & Riemsma RP (2008): Spinal fixation surgery for acute traumatic spinal cord injury. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 8 | Bellamy N, Campbell J, Welch V, Gee TL, Bourne R & Wells GA (2006): Viscosupplementation for the treatment of osteoarthritis of the knee. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 9 | Bennett MH, Feldmeier J, Hampson NB, Smee R & Milross C (2016): Hyperbaric oxygen therapy for late radiation tissue injury. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 10 | Benson D, Klain M, Braslow A, <i>et al.</i> (1996): Future directions for resuscitation research .1. Advanced airway control measures. <i>Resuscitation</i> 32: 51–62. | title | Not relevant |
| 11 | Benumof JL (1991): Management of the difficult adult airway. With special emphasis on awake tracheal intubation. <i>Anesthesiology</i> 75: 1087–1110. | title | Not relevant |
| 12 | Bezak BJ, Arce KA, Jacob A & Van Ess J (2016): Orthognathic Surgery in Patients With Congenital Myopathies and Congenital Muscular Dystrophies: Case Series and Review of the Literature. <i>Journal of Oral and Maxillofacial Surgery</i> 74: 601–609. | title | Not relevant |
| 13 | Bierma-Zeinsträ SM, Brinks A, Verhagen AP, Van Rijn RM, Koes BW & Verhaar JA (2011): Interventions for lateral hip pain (tendinopathy or bursitis). <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 14 | Bilkay U, Tiftikcioglu YO & Mezili C (2010): Management of Nasal Deformity in Osteogenesis Imperfecta. <i>Journal of Craniofacial Surgery</i> 21: 1465–1467. | title | Not relevant |
| 15 | Bloch KE (1997): Clinical significance of snoring. <i>Schweizerische Medizinische Wochenschrift</i> 127: 170–175. | title | Not relevant |
| 16 | Borrie FR, Bearn DR, Innes NP & Iheozor-Ejiofor Z (2015): Interventions for the cessation of non-nutritive sucking habits in children. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 17 | Brevi B, Di Blasio A, Di Blasio C, Piazza F, D'Ascanio L & Sesenna E (2015): Which cephalometric analysis for maxillo-mandibular surgery in patients with obstructive sleep apnoea syndrome? <i>Acta Otorhinolaryngologica Italica</i> 35: 332–337. | title | Not relevant |
| 18 | Brignardello-Petersen R, Carrasco-Labra A, Araya I, Yanine N, Cordova Jara L & Villanueva J (2015): Antibiotic prophylaxis for preventing infectious complications in orthognathic surgery. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 19 | Byrne M, Chan JCY & O'Broin E (2014): Perceptions and satisfaction of aesthetic outcome following secondary cleft rhinoplasty: evaluation by patients versus health professionals. <i>J Craniomaxillofac Surg</i> 42: 1062–1070. | title | Not relevant |
| 20 | Camacho M, Certal V, Abdulatif J, Zaghi S, Ruoff CM, Capasso R & Kushida CA (2015): Myofunctional Therapy to Treat Obstructive Sleep Apnea: A Systematic Review and Meta-analysis. <i>Sleep</i> 38: 669–675. | title | Not relevant |
| 21 | Camargo IB & Van Sickels JE (2015): Surgical complications after implant placement. <i>Dent Clin North Am</i> 59: 57–72. | title | Not relevant |
| 22 | Camirand A, Doucet J & Harris J (2004): Nose surgery: How to prevent a middle vault collapse - A review of 50 patients 3 to 21 years after surgery. <i>Plastic and Reconstructive Surgery</i> 114: 527–534. | title | Not relevant |
| 23 | Caruso L, Barone G, Farneti A & Caraffa A (2014): Pedicle subtraction osteotomy for the treatment of chin-on-chest deformity in a post-radiotherapy dropped head syndrome: a case report and review of literature. <i>European Spine Journal</i> 23: S634–S643. | title | Not relevant |
| 24 | Carvalho AP, Vital FM & Soares BG (2012): Exercise interventions for shoulder dysfunction in patients treated for head and neck cancer. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 25 | Castrillon EE, Ou K-L, Wang K, Zhang J, Zhou X & Svensson P (2016): Sleep bruxism: an updated review of an old problem. <i>Acta Odontologica Scandinavica</i> 74: 328–334. | title | Not relevant |
| 26 | Ceccato F, Bernkopf E & Scaroni C (2015): Sleep apnea syndrome in endocrine clinics. <i>Journal of Endocrinological Investigation</i> 38: 827–834. | title | Not relevant |
| 27 | Cedin AC, Atallah AN, Andriolo RB, Cruz OL & Pignatari SN (2012): Surgery for congenital choanal atresia. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 28 | Chambers HG. Advances in cerebral palsy. <i>Current Opinion in Orthopaedics</i> . 2002;13(6):424-31. | title | Not relevant |
| 29 | Chan E-Y, Fransen M, Parker DA, Assam PN & Chua N (2014): Femoral nerve blocks for acute postoperative pain after knee replacement surgery. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 30 | Chan KK, Glennly A-M, Weldon JC, Furness S, Worthington HV & Wakeford H (2015): Interventions for the treatment of oral and oropharyngeal cancers: targeted therapy and immunotherapy. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 31 | Chate R (1994): The Burden of Proof - a Critical-Review of Orthodontic Claims Made by Some General-Practitioners. <i>American Journal of Orthodontics and Dentofacial Orthopedics</i> 106: 96–105. | title | Not relevant |
| 32 | Christovam IO, Lisboa CO, Ferreira DMTP, Cury-Saramago AA & Mattos CT (2016): Upper airway dimensions in | title | Not relevant |

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| | patients undergoing orthognathic surgery: a systematic review and meta-analysis. International Journal of Oral and Maxillofacial Surgery 45: 460–471. | | |
| 33 | Coghlan JA, Buchbinder R, Green S, Johnston RV & Bell SN (2008): Surgery for rotator cuff disease. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 34 | Cohen system. review, Burstein FD & Williams JK (1999): The role of distraction osteogenesis in the management of craniofacial disorders. Ann Acad Med Singap 28: 728–738. | title | Not relevant |
| 35 | Coppola C & Maffulli N (1999): Limb shortening for the management of leg length discrepancy. J R Coll Surg Edinb 44: 46–54. | title | Not relevant |
| 36 | Culebras A (2007): Cerebrovascular disease and the pathophysiology of obstructive sleep apnea. Current Neurology and Neuroscience Reports 7: 173–179. | title | Not relevant |
| 37 | Dao TT & Lavigne GJ (1998): Oral splints: the crutches for temporomandibular disorders and bruxism? Crit Rev Oral Biol Med 9: 345–361. | title | Not relevant |
| 38 | De Backer JW, Vos WG, Verhulst SL & De Backer W (2008): Novel imaging techniques using computer methods for the evaluation of the upper airway in patients with sleep-disordered breathing: A comprehensive review. Sleep Medicine Reviews 12: 437–447. | title | Not relevant |
| 39 | de Beer D & Bingham R (2011): The child with facial abnormalities. Curr Opin Anaesthesiol 24: 282–288. | title | Not relevant |
| 40 | de Oliveira Carvalho PE, da Silva MVM, Rodrigues OR & Cataneo AJM (2014): Surgical interventions for treating pectus excavatum. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 41 | de Souza RF, Lovato da Silva CH, Nasser M, Fedorowicz Z & Al-Muharrqi MA (2012): Interventions for the management of temporomandibular joint osteoarthritis. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 42 | de Souza RF, Travess H, Newton T & Marchesan MA (2015): Interventions for treating traumatised ankylosed permanent front teeth. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 43 | Delaire J (1997): Maxillary development revisited: Relevance to the orthopaedic treatment of Class III malocclusions. European Journal of Orthodontics 19: 289–311. | title | Not relevant |
| 44 | Denolf PL, Vanderveken OM, Marklund ME & Braem MJ (2016): The status of cephalometry in the prediction of non-CPAP treatment outcome in obstructive sleep apnea patients. Sleep Med Rev 27: 56–73. | title | Not relevant |
| 45 | Derry CJ, Derry S & Moore RA (2014): Caffeine as an analgesic adjuvant for acute pain in adults. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 46 | Douglas N (1988): Respiratory Events During Sleep Amiens - 19th-20th November, 1987. European Respiratory Journal 1: 473–475. | title | Not relevant |
| 47 | Dunn AL, Buffa EA, Hanshaw DM & Farrell M (2012): Osteosarcoma at the site of titanium orthopaedic implants in a dog. Australian Veterinary Journal 90: 39–43. | title | Not relevant |
| 48 | El-Angbawi A, McIntyre GT, Fleming PS & Beam DR (2015): Non-surgical adjunctive interventions for accelerating tooth movement in patients undergoing fixed orthodontic treatment. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 49 | El-Bialy T & Alhadlaq A (2013): New Therapeutics in Promoting and Modulating Mandibular Growth in Cases with Mandibular Hypoplasia. Biomed Research International 789679. | title | Not relevant |
| 50 | El-Orbany M & Woehlick HJ (2009): Difficult mask ventilation. Anesth Analg 109: 1870–1880. | title | Not relevant |
| 51 | Figueroa AA, Polley JW, Friede H & Ko EW (2004): Long-term skeletal stability after maxillary advancement with distraction osteogenesis using a rigid external distraction device in cleft maxillary deformities. Plastic and Reconstructive Surgery 114: 1382–1392. | title | Not relevant |
| 52 | Fleury B (2006): [Which mandibular advancement splint should be chosen and how should effective advancement be defined?]. Rev Mal Respir 23 Spec No 2: 7S55-7S57. | title | Not relevant |
| 53 | Flores-Mir C, Korayem M, Heo G, Witmans M, Major MP & Major PW (2013): SYSTEMATIC REVIEW Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome A systematic review and meta-analysis. Journal of the American Dental Association 144: 269–277. | title | Not relevant |
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| 57 | Furness S, Glenny A-M, Worthington HV, <i>et al.</i> (2011): Interventions for the treatment of oral cavity and oropharyngeal cancer: chemotherapy. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 58 | Gami AS, Caples SM & Somers VK (2003): Obesity and obstructive sleep apnea. Endocrinology and Metabolism Clinics of North America 32: 869–+. | title | Not relevant |
| 59 | Gelb ML (2014): Airway centric TMJ philosophy. Journal of the California Dental Association 42: 551-62–2. | title | Not relevant |
| 60 | Giles TL, Lasserson TJ, Smith B, White J, Wright JJ & Cates CJ (2006): Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 61 | Glassman B & Gonzalez B (2005): The role of the dentist in the therapeutic support of sleep apnea. Int J Orthod Milwaukee 16: 31–35. | title | Not relevant |
| 62 | Goga D, Fassio E, Bonin B, Durand JL & Sirinelli D (1998): [Congenital stenosis of the piriform aperture: a cause of respiratory distress in newborn infants. Review of the literature, from 2 cases]. Rev Stomatol Chir Maxillofac 99: 203–206. | title | Not relevant |
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| 65 | Gola R, Guyot L, Richard O & Layoun W (2002): [Look and nasal ventilation]. Ann Chir Plast Esthet 47: 316–328. | title | Not relevant |

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| 66 | Goode RL (2007): Success and failure in treatment of sleep apnea patients. Otolaryngologic Clinics of North America 40: 891–+. | title | Not relevant |
| 67 | Gordon JM, Rosenblatt M, Witmans M, Carey JP, Heo G, Major PW & Flores-Mir C (2009): Rapid Palatal Expansion Effects on Nasal Airway Dimensions as Measured by Acoustic Rhinometry A Systematic Review. Angle Orthodontist 79: 1000–1007. | title | Not relevant |
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| 72 | Grusovin MG, Coulthard P, Worthington HV, George P & Esposito M (2010): Interventions for replacing missing teeth: maintaining and recovering soft tissue health around dental implants. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
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| 76 | Guijarro-Martinez R & Swennen GRJ (2011): Cone-beam computerized tomography imaging and analysis of the upper airway: a systematic review of the literature. International Journal of Oral and Maxillofacial Surgery 40: 1227–1237. | title | Not relevant |
| 77 | Gupta RK, Jadhav V, Gupta A, Sanghvi B, Shah H & Parekar S (2008): Congenital alveolar fusion. Journal of Pediatric Surgery 43: 1421–1425. | title | Not relevant |
| 78 | Handoll HH & Brorson S (2015): Interventions for treating proximal humeral fractures in adults. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 79 | Hasnat MJ & Rice JE (2015): Intrathecal baclofen for treating spasticity in children with cerebral palsy. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
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| 82 | Hopper RA (2012): New trends in cranio-orbital and midface distraction for craniofacial dysostosis. Curr Opin Otolaryngol Head Neck Surg 20: 298–303. | title | Not relevant |
| 83 | Hounsborne J, Nicholson A, Greenhalgh J, Cook TM, Smith AF & Lewis system. review (2016): Nitrous oxide-based versus nitrous oxide-free general anaesthesia and accidental awareness during general anaesthesia in surgical patients. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 84 | Hunter AGW, Bankier A, Rogers JG, Sillence D & Scott CI (1998): Medical complications of achondroplasia: a multicentre patient review. Journal of Medical Genetics 35: 705–712. | title | Not relevant |
| 85 | Huynh NT, Emami E, Helman JI & Chervin RD (2014): Interactions between sleep disorders and oral diseases. Oral Diseases 20: 236–245. | title | Not relevant |
| 86 | Huynh NT, Rompré PH, Montplaisir JY, Manzini C, Okura K & Lavigne GJ (2006): Comparison of various treatments for sleep bruxism using determinants of number needed to treat and effect size. Int J Prosthodont 19: 435–441. | title | Not relevant |
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| 88 | Infosino A (2002): Pediatric upper airway and congenital anomalies. Anesthesiol Clin North America 20: 747–766. | title | Not relevant |
| 89 | Iwasaki T & Yamasaki Y (2014): Relation between maxillofacial form and respiratory disorders in children. Sleep and Biological Rhythms 12: 2–11. | title | Not relevant |
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| 93 | Jambi S, Thiruvengkatachari B, O'Brien KD & Walsh T (2013): Orthodontic treatment for distalising upper first molars in children and adolescents. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
| 94 | Jambi S, Walsh T, Sandler J, Benson PE, Skeggs RM & O'Brien KD (2014): Reinforcement of anchorage during orthodontic brace treatment with implants or other surgical methods. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | title | Not relevant |
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| 96 | Jones SF & Brito V (2014): Noncontinuous Positive Airway Pressure Therapies for Obstructive Sleep Apnea. Seminars in Respiratory and Critical Care Medicine 35: 613–620. | title | Not relevant |
| 97 | Joosten SA, O'Driscoll DM, Berger PJ & Hamilton GS (2014): Supine position related obstructive sleep apnea in adults: Pathogenesis and treatment. Sleep Medicine Reviews 18: 7–17. | title | Not relevant |

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| 99 | Kamata S (1996): [Recent advance in head and neck cancer surgery]. <i>Gan To Kagaku Ryoho</i> 23: 265–270. | title | Not relevant |
| 100 | Kanaya A, Yasuda T, Kojima A, Saishu T & Kurosawa S (2011): [Airway management in a patient with Williams syndrome]. <i>Masui</i> 60: 1176–1179. | title | Not relevant |
| 101 | Katalinic OM, Harvey LA, Herbert RD, Moseley AM, Lannin NA & Schurr K (2010): Stretch for the treatment and prevention of contractures. <i>Cochrane Database of Systematic Reviews</i> . John Wiley & Sons, Ltd. | title | Not relevant |
| 102 | Kato A, Hulse KE, Tan BK & Schleimer RP (2013): B-lymphocyte lineage cells and the respiratory system. <i>J Allergy Clin Immunol</i> 131: 933–957; quiz 958. | title | Not relevant |
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| 104 | Katyal V, Pamula Y, Martin AJ, Daynes CN, Kennedy JD & Sampson WJ (2013): Craniofacial and upper airway morphology in pediatric sleep-disordered breathing: Systematic review and meta-analysis. <i>American Journal of Orthodontics and Dentofacial Orthopedics</i> 143: 20-U204. | title | Not relevant |
| 105 | Katz ES, Mitchell RB & D'Ambrosio CM (2012): Obstructive Sleep Apnea in Infants. <i>American Journal of Respiratory and Critical Care Medicine</i> 185: 805–816. | title | Not relevant |
| 106 | Khamashta-Ledezma L & Naini FB (2014): Systematic review of changes in maxillary incisor exposure and upper lip position with Le Fort I type osteotomies with or without cinch sutures and/or VY closures. <i>International Journal of Oral and Maxillofacial Surgery</i> 43: 46–61. | title | Not relevant |
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| 363 | Prinsell JR (2002): Maxillomandibular advancement surgery for obstructive sleep apnea syndrome. J Am Dent Assoc 133: 1489-1497-1540. | abstract | Not system. review |
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| 397 | Sutherland K, Vanderveken OM, Tsuda H, Marklund M, Gagnadoux F, Kushida CA & Cistulli PA (2014): Oral appliance treatment for obstructive sleep apnea: an update. J Clin Sleep Med 10: 215–227. | abstract | Not system. review |
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| 400 | Tauman R & Gozal D (2011): Obstructive sleep apnea syndrome in children. <i>Expert Review of Respiratory Medicine</i> 5: 425–440. | abstract | Not relevant |
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| 402 | Trang H (2006): [Obstructive sleep apnea treatment in children]. <i>Rev Mal Respir</i> 23 Spec No 2: 7S128-127S130. | abstract | Not system. review |
| 403 | Triplett W, Lund B, Westbrook P & Olsen K (1989): Obstructive Sleep-Apnea Syndrome in Patients with Class-II Malocclusion. <i>Mayo Clinic Proceedings</i> 64: 644–652. | abstract | Not relevant |
| 404 | Troell RJ, Powell NB & Riley RW (1998): Hypopharyngeal airway surgery for obstructive sleep apnea syndrome. <i>Seminars in Respiratory and Critical Care Medicine</i> 19: 175–183. | abstract | Not system. review |
| 405 | Troell RJ, Riley RW, Powell NB & Li K (1998): Surgical management of the hypopharyngeal airway in sleep disordered breathing. <i>Otolaryngologic Clinics of North America</i> 31: 979–+. | abstract | Not system. review |
| 406 | Tucker Woodson B (2008): Structural effectiveness of pharyngeal sleep apnea surgery. <i>Sleep medicine reviews</i> 12: 463–79. | abstract | Not relevant |
| 407 | Urquhart DS (2013): Investigation and management of childhood sleep apnoea. <i>Hippokratia</i> 17: 196–202. | abstract | Not relevant |
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| 409 | Verse T & Hoermann K (2011): The Surgical Treatment of Sleep-Related Upper Airway Obstruction. <i>Deutsches Arzteblatt International</i> 108: 216-U37. | abstract | Not system. review |
| 410 | Verse T, Bodlaj R, de la Chaux R, <i>et al.</i> (2009): Guideline: Treatment of obstructive sleep apnea in adults. <i>Hno</i> 57: 1136–+. | abstract | Practice guideline |
| 411 | Verse T, de la Chaux R, Dreherz A, <i>et al.</i> (2008): Guideline: Treatment of adult obstructive sleep apnea. <i>Laryngo-Rhino-Otologie</i> 87: 192–204. | abstract | Practice guideline |
| 412 | Villa MP, Miano S & Rizzoli A (2012): Mandibular advancement devices are an alternative and valid treatment for pediatric obstructive sleep apnea syndrome. <i>Sleep and Breathing</i> 16: 971–976. | abstract | Not relevant |
| 413 | Viviano JS (2004): Assessing orthotic normalization of pharyngeal dynamics. <i>Cranio-the Journal of Craniomandibular Practice</i> 22: 192–208. | abstract | Not relevant |
| 414 | Vlastos IM & Hajioannou JK (2010): Clinical practice - Diagnosis and treatment of childhood snoring. <i>European Journal of Pediatrics</i> 169: 261–267. | abstract | Not relevant |
| 415 | Vukcevic M (2011): [Modalities in the treatment of obstructive breathing in sleep]. <i>Glas system. reviewpska akademija nauka i umetnosti Odeljenje medicinskih nauka</i> 75–83. | abstract | Not relevant |
| 416 | Waite PD (1998): Obstructive sleep apnea - A review of the pathophysiology and surgical management. <i>Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics</i> 85: 352–361. | abstract | Not system. review |
| 417 | Weaver TE, Calik MW, Farabi SS, Fink AM, Galang-Boquiren MT, Kapella MC, Prasad B & Carley DW (2014): Innovative treatments for adults with obstructive sleep apnea. <i>Nat Sci Sleep</i> 6: 137–147. | abstract | Not relevant |
| 418 | White DP (2006): Sleep apnea. <i>Proceedings of the American Thoracic Society</i> 3: 124–8. | abstract | Not relevant |
| 419 | Won CHJ, Li KK & Guilleminault C (2008): Surgical treatment of obstructive sleep apnea: upper airway and maxillomandibular surgery. <i>Proceedings of the American Thoracic Society</i> 5: 193–9. | abstract | Not relevant |
| 420 | Woodson BT (2008): Structural effectiveness of pharyngeal sleep apnea surgery. <i>Sleep Medicine Reviews</i> 12: 463–479. | abstract | Not relevant |
| 421 | Woodson BT (2010): Non-pressure therapies for obstructive sleep apnea: surgery and oral appliances. <i>Respir Care</i> 55: 1314–1321; discussion 1321. | abstract | Not relevant |
| 422 | Young D & Collop N (2014): Advances in the Treatment of Obstructive Sleep Apnea. <i>Current Treatment Options in Neurology</i> 16: 305. | abstract | Not system. review |
| 423 | Zeng X & Gao X (2009): [Current research of dentistry on obstructive sleep apnea hypopnea syndrome]. <i>Beijing da xue xue bao Yi xue ban = Journal of Peking University Health sciences</i> 41: 10–5. | abstract | Not relevant |
| 424 | [No authors] Corrections to "Comparison of the effects of continuous positive airway pressure and mandibular advancement devices on sleepiness in patients with obstructive sleep apnoea: A network meta-analysis"[<i>Lancet Respir Med</i> (2015) 3, 869-878.]. <i>The Lancet Respiratory Medicine</i> . 2015;3(12):e44. | abstract | Not relevant |
| 425 | Aurora RN, Casey KR, Kristo D, Auerbach S, Bista system. review, Chowdhuri S, <i>et al.</i> Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. <i>Sleep</i> . 2010;33(10):1408-13. | full text | Not system. review |
| 426 | Bratton DJ, Gaisl T, Wons AM & Kohler M (2015): CPAP vs Mandibular Advancement Devices and Blood Pressure in Patients With Obstructive Sleep Apnea A Systematic Review and Meta-analysis. <i>Jama-Journal of the American Medical Association</i> 314: 2280–2293. | full text | Other outcome |
| 427 | Iftikhar IH, Hays ER, Iverson MA, Magalang UJ, Maas AK. Effect of oral appliances on blood pressure in obstructive sleep apnea: A systematic review and meta-analysis. <i>Journal of Clinical Sleep Medicine</i> . 2013;9(2):165-74. | full text | Other outcome |
| 428 | Johal A, Fleming PS, Manek S & Marinho VCC (2015): Mandibular advancement splint (MAS) therapy for obstructive sleep apnoea-an overview and quality assessment of systematic reviews. <i>Sleep and Breathing</i> 19: 1101–1108. | full text | Overview of system. review |
| 429 | Kezirian EJ & Goldberg AN (2006): Hypopharyngeal surgery in obstructive sleep apnea - An evidence-based medicine review. <i>Archives of Otolaryngology-Head & Neck Surgery</i> 132: 206–213. | full text | Not relevant |
| 430 | Martínez-González J-M, Martínez-Rodríguez N, Arias-Irimia O, Martín-Arés M & Barona-Dorado C (2010): Odontostomatological therapeutic possibilities in patients with sleep apnea. <i>Med Oral Patol Oral Cir Bucal</i> 15: e605-610. | full text | Not system. review |
| 431 | Mattos CT, Vilani GNL, Sant'Anna EF, Ruellas ACO & Maia LC (2011): Effects of orthognathic surgery on oropharyngeal airway: a meta-analysis. <i>Int J Oral Maxillofac Surg</i> 40: 1347–1356. | full text | Not relevant |
| 432 | Maurer JT (2009): Update on surgical treatment for sleep apnoea. <i>Swiss Medical Weekly</i> 139: 624–629. | full text | Not system. review |
| 433 | Maurer JT (2010): Surgical treatment of obstructive sleep apnea: standard and emerging techniques. <i>Current</i> | full text | Not system. review |

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| | Opinion in Pulmonary Medicine 16: 552–558. | | |
| 434 | Mohsenin N, Mostofi MT & Mohsenin V (2003): The role of oral appliances in treating obstructive sleep apnea. J Am Dent Assoc 134: 442–449. | full text | Not system. review |
| 435 | Ngiam J, Balasubramaniam R, Darendeliler MA, Cheng AT, Waters K & Sullivan CE (2013): Clinical guidelines for oral appliance therapy in the treatment of snoring and obstructive sleep apnoea. Aust Dent J 58: 408–419. | full text | Not system. review |
| 436 | Okuno K, Pliska BT, Hamoda M, Lowe AA & Almeida FR (2016): Prediction of oral appliance treatment outcomes in obstructive sleep apnea: A systematic review. Sleep Med Rev 30: 25–33. | full text | No eligible outcome |
| 437 | Pirsig W & Verse T (2000): Long-term results in the treatment of obstructive sleep apnea. European Archives of Oto-Rhino-Laryngology 257: 570–577. | full text | Not system. review |
| 438 | Prinsell JR (2012): Primary and Secondary Telegnathic Maxillomandibular Advancement, With or Without Adjunctive Procedures, for Obstructive Sleep Apnea in Adults: A Literature Review and Treatment Recommendations. Journal of Oral and Maxillofacial Surgery 70: 1659–1677. | full text | Not system. review |
| 439 | Rosário HD, Oliveira GMS, Freires IA, de Souza Matos F & Paranhos LR (2016): Efficiency of bimaxillary advancement surgery in increasing the volume of the upper airways: a systematic review of observational studies and meta-analysis. Eur Arch Otorhinolaryngol. | full text | Not relevant |
| 440 | Saffer F, Lubianca Neto JF, Lubianca JFL, Rösing C, Dias C & Closs L (2015): Predictors of success in the treatment of obstructive sleep apnea syndrome with mandibular repositioning appliance: a systematic review. Int Arch Otorhinolaryngol 19: 80–85. | full text | No eligible outcome |
| 441 | Saffer F, Lubianca Neto JF, Rösing C, Dias C, Closs L. Erratum: Predictors of Success in the Treatment of Obstructive Sleep Apnea Syndrome with Mandibular Repositioning Appliance: A Systematic Review (International Archives of Otorhinolaryngology (2015) 19 367). International Archives of Otorhinolaryngology. 2014;19(4):367. | full text | Not relevant |
| 442 | Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F & Menn S (1995): Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 18: 501–510. | full text | No eligible primary studies |
| 443 | Senn O, Bloch KE, Iseli A, Hochban W, Finkelstein Y, Boudewyns, <i>et al.</i> . Oral appliances for the treatment of snoring and obstructive sleep apnea. Oto-Rhino-Laryngologia Nova. 2001;11(4):168-77. | full text | Not system. review |
| 444 | Sommer JU, Maurer JT, Hörmann K & Stuck BA (2012): [Randomized controlled trials in the surgical treatment of obstructive sleep apnea]. HNO 60: 294–299. | full text | Not system. review |
| 445 | Sundaram S, Bridgman SA, Lim J & Lasserson TJ (2005): Surgery for obstructive sleep apnoea. Cochrane Database Syst Rev CD001004. | full text | No eligible intervention |
| 446 | Sundaram S, Lim J & Lasserson TJ (2005): Surgery for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd. | full text | No eligible intervention |
| 447 | Sujanska A, Durdik P, Jesenák M, Banovcin P, Rabasco J, Vitelli O, <i>et al.</i> . Obstructive sleep apnea syndrome in children - the recent view on the treatment. Advances in Respiratory Therapy Research. 2014:177-90. | full text | Book chapter |
| 448 | Verse T, Hierl T. Maxillofacial surgeries. Surgery for Sleep Disordered Breathing. 2010:167-92. | full text | Book chapter |
| 449 | Zancanella E, Haddad FM, Oliveira LAMP, Nakasato A, Duarte BB, Soares CFP, <i>et al.</i> . Obstructive sleep apnea and primary snoring: Treatment. Brazilian Journal of Otorhinolaryngology. 2014;80(1 SUPPL. 1):S17-S28. | full text | Not system. review |
| 450 | Taylor BA, Brace M & Hong P (2014): Upper airway outcomes following midface distraction osteogenesis: a systematic review. J Plast Reconstr Aesthet Surg 67: 891–899. | full text | Syndromic patients |
| 451 | Al-Jewair TS; Gaffar BO; Flores-Mir C. - Quality Assessment of Systematic reviews on the Efficacy of Oral Appliance Therapy for Adult and Pediatric Sleep-Disordered Breathing. - J Clin Sleep Med 2016;12(8):1175–1183. | full text | Not system. review |
| 452 | Sánchez-de-la-Torre M, Barbé F. What treatment wins in the battle against sleepiness? The Lancet Respiratory Medicine. 2015;3(11):828-9. | full text | Not system. review |
| 453 | Kotecha B (2006): Managing snoring and severe OSA. The Practitioner 250: 49–50. | full text | Not system. review |
| 454 | Laniado N, Goldberg R & Fry JM (1993): Addressing snoring and obstructive sleep apnea: a problem often overlooked in women. Compendium (Newtown, Pa) 14: passim-1572, 1574, 1576 passim. | full text | Not system. review |
| 455 | Monod M-L & Pasche P (2002): [Sleep apnea syndrome and snoring: what is the role of surgery?]. Revue medicale de la Suisse romande 122: 273–6. | full text | Not system. review |
| 456 | Simonds AK (2001): Managing obstructive sleep apnoea. Practitioner 245: 117–120. | full text | Not system. review |
| 457 | Tardif C (2000): [Treatment of sleep apnea syndromes]. Presse Med 29: 1083–1090. | full text | Not system. review |
| 458 | Petitjean T, Chammas N, Langevin B, Philit F & Robert D (2000): Principles of mandibular advancement device applied to the therapeutic of snoring and sleep apnea syndrome. Sleep 23 Suppl 4: S166-171. | full text | Not system. review |
| 459 | Petitjean T, Garcia Tejero MT, Langevin B, Philit F & Robert D (2000): [Mandibular advancement orthoses used in the treatment of obstructive sleep apnea syndrome]. Rev Mal Respir 17 Suppl 3: S69-79. | full text | Not system. review |
| 460 | Petitjean T, Langevin B, Idrissi SM, Philit F, Garcia Tejero MT & Robert D (2002): [Treatment of obstructive sleep apnea syndrome with mandibular advancement appliances]. Rev Stomatol Chir Maxillofac 103: 170–180. | full text | Not system. review |
| 461 | Main C, Liu Z, Welch K, Weiner G, Jones SQ & Stein K (2009): Surgical procedures and non-surgical devices for the management of non-apnoeic snoring: a systematic review of clinical effects and associated treatment costs. Health Technol Assess 13: iii, xi–xiv, 1-208. | full text | Not relevant |
| 462 | Randerath WJ, Verbraecken J, Andreas S, <i>et al.</i> . (2011): Non-CPAP therapies in obstructive sleep apnoea. Eur Respir J 37: 1000–1028. | full text | Double report |
| 463 | Randerath W, Bauer M, Blau A, <i>et al.</i> . (2007): [Are there alternative therapeutical options other than CPAP in the treatment of the obstructive sleep apnea syndrome]. Pneumologie (Stuttgart, Germany) 61: 458–66. | full text | Not system. review |
| 464 | Ferguson KA, Cartwright R, Rogers R & Schmidt-Nowara W (2006): Oral appliances for snoring and obstructive sleep apnea: A review. Sleep 29: 244–262. | full text | Not system. review |
| 465 | Attias E, Chabolle F, Crampette L, <i>et al.</i> . (2000): Clinical and economic evaluation of surgery in the treatment of chronic obstructive sleep apnea. Revue Des Maladies Respiratoires 17: S5–S48. | No abstract found | |
| 466 | Hochban W, Brandenburg U & Peter JH (1995): [Surgical treatment of obstructive sleep apnea by maxillary and mandibular osteotomy]. Fortschritte der Kiefer- und Gesichtschirurgie 40: 65–72. | No abstract found | |

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| 467 | Takahashi Y, Shimizu T & Hishikawa Y (1993): [Treatment of sleep apnea syndrome]. Kokyu To Junkan 41: 841–844. | No abstract found |
| 468 | Levy P, Bettega G, Pepin JL. Surgical management options for snoring and sleep apnoea. European Respiratory Monograph. 1998;3(10):205-26. | No full-text found |

eTable 4. Methodological quality of included systematic reviews.

| Nr. | Citation | 1. Was an 'a priori' design provided? | 2. Was there duplicate study selection and data extraction? | 3. Was a comprehensive literature search performed? | 4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? | 5. Was a list of studies (included and excluded) provided? | 6. Were the characteristics of the included studies provided? | 7. Was the scientific quality of the included studies assessed and documented? | 8. Was the scientific quality of the included studies used appropriately in formulating conclusions? | 9. Were the methods used to combine the findings of studies appropriate? | 10. Was the likelihood of publication bias assessed? | 11. Was the conflict of interest included? |
|-----|--------------------------------------|---------------------------------------|---|---|---|--|---|--|--|--|--|--|
| 1 | Abdullatif (2016) (e11) | No | No | Yes | Yes | No | Yes | Yes | No | Yes | Yes | No |
| 2 | Ahrens (2011) (e12) | No | Yes | Yes | No | No | No ^{*2} | No | No | NA | No | No |
| 3 | Bartolucci (2016) (e13) | No | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | No |
| 4 | Bratton (2015) (e14) | Yes | Yes | Yes | No | No | Yes | Yes | No | Yes | Yes | No |
| 5 | Bridgman and Dunn (2000) (e15) | No | Yes | Yes | Yes | No | No | Yes | Yes | NA | No | No |
| 6 | Caldas (2009) (e16) | No | Yes | No | No | No | Yes | Yes | No | NA | No | No |
| 7 | Camacho (2015) (e17) | No | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | No |
| 8 | Caples (2010) (e18) | Yes | Yes | Yes | No | No | Yes | Yes | Yes | No | No | No |
| 9 | Carvalho (2007, 2016) (e19, e20) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | NA | Yes | No |
| 10 | Health Quality Ontario (2009) (e21) | No | No | Yes | No | No | Yes | Yes | Yes | Yes | No | No |
| 11 | Hoekema (2004) (e22) | No | No | Yes | Yes | No | Yes | Yes | Yes | No | No | No |
| 12 | Holty and Guilleminault (2010) (e23) | No | Yes | No | No | No | Yes | No | No | No | No | No |
| 13 | Hsieh and Liao (2013) (e24) | No | Yes | No | No | No | Yes | Yes | Yes | NA | No | No |
| 14 | Huynh (2016) (e25) | Yes | Yes | Yes | No | Yes | Yes | No ^{*3} | Yes | No | No | No |
| 15 | Knudsen (2015) (e26) | No | No | Yes | No | No | No | No | No | Yes | Yes | No |
| 16 | Li (2013) (e27) | Yes | Yes | Yes | No | No | Yes | Yes | No | Yes | Yes | No |
| 17 | Lim (2004) (e28) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | No |
| 18 | Machado-Júnior (2016) (e29) | No | No | No | No | No | Yes | No | No | No | No | No |
| 19 | Marcus (2012) (e30) | No | No | Yes | No | No | No | Yes | Yes | NA | No | No |
| 20 | Marklund (2012) (e31) | No | No | Yes | No | No | Yes | Yes | Yes | NA | No | No |
| 21 | Nazarali (2015) (e32) | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| 22 | Okuno (2014) (e33) | No | Yes | Yes | No | No | Yes | Yes | No | Yes | Yes | No |
| 23 | Pirklbauer (2011) (e34) | No | No | No | No | No | Yes | Yes | No | NA | No | No |
| 24 | Ramar (2015) (e35) | No | No | Yes | No | No | No | Yes | Yes | Yes | Yes | No |
| 25 | Serra-Torres (2016) (e36) | No | No | Yes | No | No | Yes | Yes | No | NA | No | No |
| 26 | Sharples (2016) (e37) | No | Yes | Yes | No | No | No | Yes | No | Yes | Yes | No |
| 27 | Sher (1996) (e38) ^{*1} | Yes | Yes | No | No | No | No | No | No | NA | No | No |
| 28 | Zaghi (2016) (e39) | No | Yes | Yes | No | No | No | Yes | No | Yes | No ^{*4} | No |
| 29 | Zhu (2015) (e40) | No | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | No |

NA, not applicable.

^{*1} Data extracted only on MMA

^{*2} Dead link

^{*3} Inappropriate tool

^{*4} Funnel-like plot provided, but no statistical confirmation

eTable 5. List of included primary studies.

| | |
|----|---|
| 1 | Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: a randomized, placebo-controlled trial. <i>Respiration</i> . 2011;81(5):411-9. |
| 2 | Barnes M, McEvoy RD, Banks S, Tarquinio N, Murray CG, Vowles N, Pierce RJ. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. <i>Am J Respir Crit Care Med</i> . 2004 Sep 15;170(6):656-64. |
| 3 | Blanco J, Zamarrón C, Abeleira Pazos MT, Lamela C, Suarez Quintanilla D. Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome. <i>Sleep Breath</i> . 2005 Mar;9(1):20-5. |
| 4 | Bloch KE, Iseli A, Zhang JN, Xie X, Kaplan V, Stoeckli PW, Russi EW. A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. <i>Am J Respir Crit Care Med</i> . 2000 Jul;162(1):246-51. |
| 5 | Dal-Fabbro C, Garbuio S, D'Almeida V, Cintra FD, Tufik S, Bittencourt L. Mandibular advancement device and CPAP upon cardiovascular parameters in OSA. <i>Sleep Breath</i> . 2014 Dec;18(4):749-59. |
| 6 | de Britto Teixeira, Andressa Otranto, Luciana Baptista Pereira Abi-Ramia, and Marco Antonio de Oliveira Almeida. "Treatment of obstructive sleep apnea with oral appliances." <i>Progress in orthodontics</i> 14.1 (2013): 10. |
| 7 | Dort L, Brant R. A randomized, controlled, crossover study of a noncustomized tongue retaining device for sleep disordered breathing. <i>Sleep Breath</i> . 2008 Nov;12(4):369-73. |
| 8 | Durán-Cantolla J, Crovetto-Martínez R, Alkhraisat MH, Crovetto M, Municio A, Kutz R, Aizpuru F, Miranda E, Anitua E. Efficacy of mandibular advancement device in the treatment of obstructive sleep apnea syndrome: A randomized controlled crossover clinical trial. <i>Med Oral Patol Oral Cir Bucal</i> . 2015 Sep 1;20(5):e605-15. |
| 9 | Gotsopoulos H, Chen C, Qian J, Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. <i>Am J Respir Crit Care Med</i> . 2002 Sep 1;166(5):743-8. / Gotsopoulos H, Kelly JJ, Cistulli PA. Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. <i>Sleep</i> . 2004 Aug 1;27(5):934-41. / Naismith SL, Winter VR, Hickie IB, Cistulli PA. Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. <i>J Clin Sleep Med</i> . 2005 Oct 15;1(4):374-80. |
| 10 | Hans MG, Nelson S, Luks VG, Lorkovich P, Baek SJ. Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). <i>Am J Orthod Dentofacial Orthop</i> . 1997 May;111(5):562-70. |
| 11 | Johnston CD, Gleadhill IC, Cinnamond MJ, Gabbey J, Burden DJ. Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. <i>Eur J Orthod</i> . 2002 Jun;24(3):251-62. |
| 12 | Lam B, Sam K, Mok WY, Cheung MT, Fong DY, Lam JC, Lam DC, Yam LY, Ip MS. Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnoea. <i>Thorax</i> . 2007 Apr;62(4):354-9. |
| 13 | Maguire J, Steele JG, Gibson GJ, Wilson JA, Steen N, McCracken GI. Randomised cross-over study of oral appliances for snoring. <i>Clin Otolaryngol</i> . 2010 Jun;35(3):204-9. |
| 14 | Marklund M, Carlberg B, Forsgren L, Olsson T, Stenlund H, Franklin KA. Oral Appliance Therapy in Patients With Daytime Sleepiness and Snoring or Mild to Moderate Sleep Apnea: A Randomized Clinical Trial. <i>JAMA Intern Med</i> . 2015 Aug;175(8):1278-85. |
| 15 | Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. <i>Am J Respir Crit Care Med</i> . 2001 May;163(6):1457-61. |
| 16 | Petri N, Svanholt P, Solow B, Wildschjødzt G, Winkel P. Mandibular advancement appliance for obstructive sleep apnoea: results of a randomised placebo controlled trial using parallel group design. <i>J Sleep Res</i> . 2008 Jun;17(2):221-9. |
| 17 | Pitsis AJ, Darendeliler MA, Gotsopoulos H, Petocz P, Cistulli PA. Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. <i>Am J Respir Crit Care Med</i> . 2002 Sep 15;166(6):860-4. |
| 18 | Quinnell TG, Bennett M, Jordan J, Clutterbuck-James AL, Davies MG, Smith IE, Oscroft N, Pittman MA, Cameron M, Chadwick R, Morrell MJ, Glover MJ, Fox-Rushby JA, Sharples LD. A crossover randomised controlled trial of oral mandibular advancement devices for obstructive sleep apnoea-hypopnoea (TOMADO). <i>Thorax</i> . 2014 Oct;69(10):938-45. / Sharples L, Glover M, Clutterbuck-James A, Bennett M, Jordan J, Chadwick R, Pittman M, East C, Cameron M, Davies M, Oscroft N, Smith I, Morrell M, Fox-Rushby J, Quinnell T. Clinical effectiveness and cost-effectiveness results from the randomised controlled Trial of Oral Mandibular Advancement Devices for Obstructive sleep apnoea-hypopnoea (TOMADO) and long-term economic analysis of oral devices and continuous positive airway pressure. <i>Health Technol Assess</i> . 2014 Oct;18(67):1-296. |
| 19 | Rose E, Staats R, Virchow C, Jonas IE. A comparative study of two mandibular advancement appliances for the treatment of obstructive sleep apnoea. <i>Eur J Orthod</i> . 2002 Apr;24(2):191-8. |
| 20 | Villa MP, Bernkopf E, Pagani J, Broia V, Montesano M, Ronchetti R. Randomized controlled study of an oral jaw-positioning appliance for the treatment of obstructive sleep apnea in children with malocclusion. <i>Am J Respir Crit Care Med</i> . 2002 Jan 1;165(1):123-7. |

eTable 6. Overall results for the comparison of oral appliances vs placebo on the AHI.

| | | Trials | Effect | 95% CI | p | 95% PrI | τ^2 | I^2 (%) |
|--|-------------|--------|--------|---------------|--------|--------------|----------|-----------|
| Meta-analysis | MD | 12 | -11.69 | -15.38,-8.01 | <0.001 | -22.55,-0.85 | 20.15 | 93.6 |
| | | | | | | | | |
| Factor | | Trials | Effect | 95% CI | p | | τ^2 | I^2 (%) |
| Follow-up (months) | Coefficient | 11 | 0.25 | -0.24,0.75 | 0.273 | | 21.23 | 94.7 |
| | Constant | | -14.40 | -21.20,-7.61 | 0.001 | | | |
| | | | | | | | | |
| % of maximum protrusion | Coefficient | 8 | 0.03 | -0.42,0.48 | 0.870 | | 34.21 | 96.3 |
| | Constant | | -14.18 | -48.70,20.34 | 0.354 | | | |
| | | | | | | | | |
| Appliance type (thermoplastic vs impression-based) | Coefficient | 13 | 6.25 | -3.73,16.24 | 0.196 | | 17.12 | 89.4 |
| | Constant | | -12.17 | -15.68,8.66 | <0.001 | | | |
| | | | | | | | | |
| Appliance type (1- or 2-piece) | Coefficient | 9 | -0.09 | -11.25,11.08 | 0.986 | | 15.79 | 87.9 |
| | Constant | | -14.24 | -24.81,-4.30 | 0.012 | | | |
| | | | | | | | | |
| Baseline BMI (kg/m ²) | Coefficient | 12 | 1.94 | -0.84,4.72 | 0.152 | | 17.42 | 88.7 |
| | Constant | | -68.59 | -150.39,13.21 | 0.091 | | | |
| | | | | | | | | |
| Baseline AHI (events/hour) | Coefficient | 11 | -0.53 | -0.72,-0.34 | <0.001 | | 2.84 | 46.3 |
| | Constant | | 1.17 | -3.64,5.99 | 0.595 | | | |
| | | | | | | | | |
| Baseline age (years) | Coefficient | 12 | 0.44 | -1.05,1.93 | 0.524 | | 21.46 | 91.3 |
| | Constant | | -33.59 | -107.42,40.25 | 0.335 | | | |
| | | | | | | | | |
| Ratio of male patients | Coefficient | 12 | -28.65 | -78.34,21.05 | 0.228 | | 18.8 | 93.7 |
| | Constant | | 10.39 | -28.05,48.82 | 0.561 | | | |
| | | | | | | | | |
| Total sample | Coefficient | 12 | 0.14 | 0.04,0.24 | 0.010 | | 9.78 | 73.7 |
| | Constant | | -19.13 | -25.29,-12.98 | <0.001 | | | |
| | | | | | | | | |
| Trial (crossover or parallel) | Coefficient | 12 | -0.52 | -8.85,7.81 | 0.892 | | 22.5 | 94.2 |
| | Constant | | -11.38 | -18.25,4.51 | 0.004 | | | |
| | | | | | | | | |
| Data type 1 | Coefficient | 12 | -1.20 | -10.98,8.58 | 0.790 | | 22.39 | 94.2 |
| | Constant | | -11.49 | -15.81,-7.17 | <0.001 | | | |
| | | | | | | | | |
| Data type 2 | Coefficient | 12 | 8.07 | -1.72,17.86 | 0.096 | | 15.9 | 89.2 |
| | Constant | | -12.77 | -16.47,-9.07 | <0.001 | | | |
| | | | | | | | | |
| Data type 1 | Coefficient | 12 | 0.22 | -9.36,9.79 | 0.274 | | 18.15 | 90.2 |
| Data type 2 | Coefficient | | 8.12 | -2.63,18.88 | | | | |
| | Constant | | -12.82 | -17.25,-8.39 | <0.001 | | | |
| | | | | | | | | |
| | | Trials | Effect | 95% CI | p | | | |
| Reporting bias (Egger's test) | Coefficient | 12 | -1.24 | -5.35,2.87 | 0.516 | | | |

CI, Confidence Intervals; PrI, Predictive Intervals; MD, Mean Differences; BMI, body mass index; Data type 1, origin of data used in the analysis 1 (increment calculated from parallel or cross-over trials); Data type 2, origin of data used in the analysis 2 (increment calculated from final values of cross-over trials).

eTable 7. Overall results for the comparison of oral appliances vs placebo on the minimum oxygen saturation.

| | | Trials | Effect | 95% CI | p | 95% PrI | τ^2 | I^2 (%) |
|-----------------------------------|-------------|--------|--------|--------------|-------|------------|----------|-----------|
| Meta-analysis | MD | 6 | 3.33 | 1.38,5.28 | 0.007 | -1.62,8.28 | 2.19 | 96.8 |
| | | | | | | | | |
| Factor | | Trials | Effect | 95% CI | p | | τ^2 | I^2 (%) |
| Follow-up (months) | Coefficient | 5 | -0.37 | -0.61,-0.14 | 0.015 | | 0.26 | 45.6 |
| | Constant | | 7.20 | 4.69,9.70 | 0.003 | | | |
| | | | | | | | | |
| % of maximum protrusion | Coefficient | NA | | | | | | |
| | Constant | | | | | | | |
| | | | | | | | | |
| Appliance type (1- or 2-piece) | Coefficient | 5 | 2.19 | -13.13,17.51 | 0.680 | | 3.22 | 92.0 |
| | Constant | | 1.50 | -38.15,57.79 | 0.770 | | | |
| | | | | | | | | |
| Baseline BMI (kg/m ²) | Coefficient | 6 | -0.22 | -1.88,1.43 | 0.725 | | 2.70 | 92.0 |
| | Constant | | 9.82 | -38.15,57.79 | 0.600 | | | |
| | | | | | | | | |
| Baseline AHI (events/hour) | | NA | | | | | | |
| | | | | | | | | |
| Baseline age (years) | Coefficient | 6 | -0.27 | -1.14,0.60 | 0.129 | | 1.35 | 94.9 |
| | Constant | | 16.42 | -25.56,58.39 | 0.200 | | | |
| | | | | | | | | |
| Ratio of male patients | Coefficient | 6 | 22.38 | -10.19,54.96 | 0.129 | | 1.35 | 94.9 |
| | Constant | | -14.03 | -39.43,11.37 | 0.200 | | | |
| | | | | | | | | |
| Total sample | Coefficient | 6 | -0.05 | -0.11,0.00 | 0.060 | | 0.90 | 51.5 |
| | Constant | | 6.48 | 2.91,10.05 | 0.007 | | | |
| | | | | | | | | |
| Trial (crossover or parallel) | Coefficient | 6 | 1.82 | -3.34,6.97 | 0.383 | | 2.21 | 97.4 |
| | Constant | | 1.90 | -2.67,6.47 | 0.313 | | | |
| | | | | | | | | |
| Data type 1 | Coefficient | NA | | | | | | |
| | Constant | | | | | | | |
| | | | | | | | | |
| Data type 2 | Coefficient | 6 | -1.87 | -14.97,11.22 | 0.712 | | 2.69 | 97.4 |
| Cons | Constant | | 3.37 | 1.04,5.70 | 0.016 | | | |
| | | | | | | | | |
| Data type 1 | Coefficient | NA | | | | | | |
| Data type 2 | Coefficient | | | | | | | |
| Cons | Constant | | | | | | | |
| | | | | | | | | |
| | | Trials | Effect | 95% CI | p | | | |
| Reporting bias (Egger's test) | Coefficient | NA | | | | | | |

CI, Confidence Intervals; PrI, Predictive Intervals; MD, Mean Differences; NA, not applicable; BMI, body mass index; AHI, apnea hypopnea index; Data type 1, origin of data used in the analysis 1 (increment calculated from parallel or cross-over trials); Data type 2, origin of data used in the analysis 2 (increment calculated from final values of cross-over trials).

eTable 8. Overall results for the comparison of oral appliances vs placebo on the ESS.

| | | Trials | Effect | 95% CI | p | 95% PrI | τ^2 | I^2 (%) |
|--|------------------------------|--------|-------------|--------------|-------|------------|----------|-----------|
| Meta-analysis | MD | 11 | -1.18 | -2.38,0.03 | 0.055 | -4.76,2.40 | 2.12 | 60.6 |
| Factor | | Trials | Effect | 95% CI | p | | τ^2 | I^2 (%) |
| Follow-up (months) | Coefficient | 10 | 0.04 | -0.21,0.29 | 0.716 | | 3.40 | 67.2 |
| | Constant | | -1.56 | -3.95,0.83 | 0.170 | | | |
| % of maximum protrusion | Coefficient | 7 | -0.00 | -0.13,0.12 | 0.950 | | 3.36 | 66.4 |
| | Constant | | -1.48 | -10.38,7.42 | 0.686 | | | |
| Appliance type (thermoplastic or tongue suction versus impression-based) | Coefficient (thermoplast) | 10 | -0.83 | -4.38,2.72 | 0.430 | | 2.23 | 52.4 |
| | Coefficient (tongue suction) | | 2.22 | -2.34,6.78 | | | | |
| | Constant | | -1.62 | -3.31,0.08 | | 0.059 | | |
| Appliance type (1- or 2-piece) | Coefficient | 8 | 1.57 | -2.94,6.07 | 0.428 | | | |
| Constant | Constant | | -1.87 | -4.39,0.65 | 0.120 | | | |
| Baseline BMI (kg/m ²) | Coefficient | 11 | -0.21 | -1.30,0.88 | 0.671 | | 2.60 | 56.5 |
| | Constant | | 5.04 | -27.15,37.23 | 0.731 | | | |
| Baseline AHI (events/hour) | Coefficient | 9 | -0.03 | -0.16,0.10 | 0.590 | | 2.60 | 56.5 |
| | Constant | | -0.50 | -3.89,2.88 | 0.735 | | | |
| Baseline age (years) | Coefficient | 11 | -0.28 | -0.65,0.09 | 0.119 | | 1.29 | 40.9 |
| | Constant | | 12.44 | -5.41,30.29 | 0.149 | | | |
| Ratio of male patients | Coefficient | 11 | -15.22 | -33.47,3.02 | 0.092 | | 1.11 | 60.1 |
| | Constant | | 10.78 | -3.50,25.05 | 0.122 | | | |
| Total sample | Coefficient | 11 | 0.01 | -0.05,0.06 | 0.839 | | 2.70 | 58.3 |
| | Constant | | -1.47 | -4.57,1.63 | 0.312 | | | |
| Trial (crossover or parallel) | Coefficient | 11 | 1.87 | -0.76,4.50 | 0.141 | | | |
| | Constant | | -2.63 | -4.97,-0.28 | 0.032 | | | |
| Data type 1 | Coefficient | 11 | -1.87 | -4.50,0.76 | 0.141 | | 1.42 | 60.3 |
| | Constant | | -0.75 | -1.93,0.43 | 0.185 | | | |
| Data type 2 | Coefficient | 11 | -0.93 | -4.88,3.03 | 0.609 | | 2.55 | 48.2 |
| | Constant | | -1.08 | -2.49,0.32 | 0.115 | | | |
| Data type 1 | Coefficient | 11 | -2.12 | -4.80,0.55 | 0.197 | | 1.27 | 41.6 |
| Data type 2 | Coefficient | | -1.52 | -4.53,1.49 | | | | |
| | Constant | | -0.49 | -1.76,0.79 | | 0.405 | | |
| | | Trials | Coefficient | 95% CI | p | | | |
| Reporting bias (Egger's test) | Coefficient | 11 | -0.26 | -2.08,1.56 | 0.752 | | | |

CI, Confidence Intervals; PrI, Predictive Intervals; BMI, Body Mass Index; AHI, apnea hypopnea index; Data type 1, origin of data used in the analysis 1 (increment calculated from parallel or cross-over trials); Data type 2, origin of data used in the analysis 2 (increment calculated from final values of cross-over trials).